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# **PERSPECTIVES ON PRESCRIBING IN NURSING HOMES IN HELSINKI**

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ACADEMIC DISSERTATION

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# List of original publications

This dissertation is based on the following publications and some unpublished data:

- I                Hosia-Randell H, Pitkala KH. Use of psychotropic drugs in elderly nursing home residents with and without dementia in Helsinki, Finland. *Drugs Aging* 2005; 9:793-800, [Erratum appears in *Drugs Aging* 2005; 11].
  
- II               Hosia-Randell H, Suominen M, Muurinen S, Pitkala KH. Use of Laxatives among Older Nursing Home Residents in Helsinki, Finland. *Drugs Aging* 2007; 2:147-154.
  
- III              Suominen M, Hosia-Randell H, Muurinen S, Peiponen A, Routasalo P, Soini H, Suur-Uski I, Pitkala KH. Vitamin D and Calcium Supplementation among Aged Residents in Nursing Homes. *The Journal of Nutrition, Health and Aging*. 2007; 5:433-437.
  
- IV               Hosia-Randell H, Muurinen S, Pitkala KH. Exposure to Potentially Inappropriate Drugs and Drug-Drug Interactions in Elderly Nursing Home Residents in Helsinki, Finland. *Drugs Aging* 2008; 8:683-692.

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## Abbreviations

AChE	Anticholinesterase
ADE	Adverse drug event
ADR	Adverse drug reaction
ATC	Anatomical Therapeutic Chemical classification
BZD	Benzodiazepine
Ca	Calcium
CI	Confidence interval
CNS	Central nervous system
DDD	Defined Daily Dose
DDI	Drug-drug interaction
IU	International Unit
MMSE	Mini Mental State Examination
MNA	Mini Nutritional Assessment
NA	Not applicable
NH	Nursing home
NSAID	Non-steroidal anti-inflammatory drug
OBRA 87	Omnibus Budget Reconciliation Act 1987
OR	Odds ratio
PID	Potentially inappropriate drug
SD	Standard deviation
SSRI	Selective serotonin reuptake inhibitor
US	United States (of America)
µg	Microgram

# Abstract

Prescribing for older patients is challenging. The prevalence of diseases increases with advancing age and causes extensive drug use. Impairments in cognitive, sensory, social and physical functioning, multimorbidity and comorbidities, as well as age-related changes in pharmacokinetics and pharmacodynamics that impair the functional reserve of multiple systems and organs all add to the complexity of prescribing. Consequently, older people are at particular risk for adverse drug events.

This study is a cross-sectional assessment of all long-term residents aged  $\geq 65$  years in all nursing homes in Helsinki, Finland. The residents' health status was assessed and data on their demographic factors, health and medications were collected from their medical records in February 2003.

This study assesses some essential issues in prescribing for older people: psychotropic drugs (Paper I), laxatives (Paper II), vitamin D and calcium supplements (Paper III), potentially inappropriate drugs for older adults (PIDs) and drug-drug interactions (DDIs) (Paper IV), as well as prescribing in public and private nursing homes.

A resident was classified as a medication user if his or her medication record indicated a regular sequence for its dosage. Others, including those whose medication records permitted administration of the drug as needed (*pro re nata*), were classified as non-users. Mini Nutritional Assessment (MNA) was used to assess residents' nutritional status, Beers 2003 criteria to assess the use of PIDs, and the Swedish, Finnish, Interaction X-referencing database (SFINX) to evaluate their exposure to DDIs.

Of all nursing home residents in Helsinki, 82% ( $n=1987$ ) participated in studies on psychotropic drugs, laxatives, and potentially inappropriate drugs for the elderly as well as drug-drug interactions. Altogether 87% of the residents ( $n=2114$ ) participated in this study assessing the use of vitamin D and calcium supplements. The residents' mean age was 84 years, 81% were female, and 70% were diagnosed with dementia. The mean number of drugs was 7.9 per resident; 40% of the residents used  $\geq 9$  drugs per day, and were thus exposed to polypharmacy.

Of the residents, 80% received psychotropic medication, 43% received antipsychotic medication, and 45% used antidepressants. Anxiolytics were prescribed to 26%, and hypnotics to 28% of the residents. Of those residents diagnosed with dementia, 11% received antidementia drugs.

More than half (55%) of the residents received laxatives regularly. In multivariate analysis, those factors associated with regular laxative use were advanced age,

immobility, poor nutritional status, chewing problems, Parkinson's disease, and a high number of drugs. Eating snacks between meals was associated with lower risk for laxative use.

Of all participants, 33% received vitamin D supplementation, 28% received calcium supplementation, and 20% received both vitamin D and calcium. The dosage of vitamin D was rather low: 21% received vitamin D 400 IU (10 µg) or more, and only 4% received 800 IU (20 µg) or more. In multivariate analysis, residents who received vitamin D supplementation enjoyed better nutritional status, ate snacks between meals, suffered no constipation, and received regular weight monitoring.

Those residents receiving PIDs (34% of all residents) more often used psychotropic medication and were more often exposed to polypharmacy than residents receiving no PIDs. Residents receiving PIDs were less often diagnosed with dementia than were residents receiving no PIDs. The three most prevalent PIDs were short-acting benzodiazepine in greater dosages than recommended, hydroxyzine, and nitrofurantoin. These three drugs accounted for nearly 77% of all PID use.

Of all residents, less than 5% were susceptible to a clinically significant DDI. The most common DDIs were related to the use of potassium-sparing diuretics, carbamazepine, and codeine. Residents exposed to potential DDIs were younger, had more often suffered a previous stroke, more often used psychotropics, and were more often exposed to PIDs and polypharmacy than were residents not exposed to DDIs.

Residents in private nursing homes were less often exposed to polypharmacy than were residents in public nursing homes.

Long-term residents in nursing homes in Helsinki use, on average, nearly eight drugs daily. The use of psychotropic drugs in our study was notably more common than in international studies. The prevalence of laxatives equaled other prior international studies. Regardless of the known benefit and recommendation of vitamin D supplementation for elderly residing mostly indoors, the proportion of nursing home residents receiving vitamin D and calcium was surprisingly low. The use of PIDs was common among nursing home residents. PIDs increased the likelihood of DDIs. However, DDIs did not seem a major concern among the nursing home population. Monitoring PIDs and potential drug interactions could improve the quality of prescribing.



# Tiivistelmä

Ikääntyvät ihmiset sairastavat paljon ja käyttävät runsaasti lääkkeitä. Monilääkitys on yleistä erityisesti laitoksissa asuvien vanhusten keskuudessa. Toimintakyvyn ja aistitoimintojen heikkeneminen sekä ikääntymisen aiheuttamat muutokset farmakokinetiikassa ja farmakodynaamiikassa altistavat vanhuksat lääkehoidon aiheuttamille haitoille.

Tämä tutkimus on poikkileikkaus helsinkiläisten vanhainkotien yli 64-vuotiaiden pitkäaikaistasukkaiden lääkehoidosta ja siihen vaikuttavista tekijöistä. Tarkastelimme psyykelääkkeiden (osatyö I), laksatiivien (osatyö II), D-vitamiinin ja kalsiumin (osatyö III), sekä vanhuksille sopimattomien lääkkeiden (osatyö IV) käyttöä. Tarkastelimme myös lääkkeiden yhteisvaikutusten yleisyyttä (osatyö IV) sekä lääkkeiden käytön eroja julkisissa ja ostopalveluvanhainkodeissa.

Asukkaiden terveydentilaa ja lääkitystä koskevat tiedot kerättiin helmikuussa 2003. Asukas luokiteltiin lääkkeen käyttäjäksi, jos hänen sairaskertomuksestaan ilmeni määräys lääkkeen säännölliseksi annosteluksi. Asukkaiden ravitsemustila arvioitiin Mini Nutritional Assessment-menetelmällä. Vanhuksille sopimattomien lääkkeiden käyttöä arvioitiin Beersin vuonna 2003 julkaistun vanhuksille sopimattomien lääkkeiden kriteeristön avulla ja lääkkeiden yhteisvaikutuksille altistumista arviointiin SFINX-interaktiotietokannan avulla.

Psyykelääkkeiden, laksatiivien ja vanhuksille sopimattomien lääkkeiden käyttöä ja lääkkeiden yhteisvaikutuksille altistumista selvittäneisiin tutkimuksiin osallistui 82% (n=1987) helsinkiläisten vanhainkotien asukkaista. D-vitamiini- ja kalsiumvalmisteiden käytön tutkimukseen osallistui 87% (n=2114) asukkaista. Asukkaiden keski-ikä oli 84 vuotta, heistä 81% oli naisia ja 70%:lla oli dementia-diagnoosi. Asukkaiden keskimääräinen päivittäinen lääkemäärä oli lähes 8 lääkettä ja 40% asukkaista käytti päivittäin yli yhdeksää lääkettä.

Asukkaista 80% käytti psyykelääkkeitä. Antipsykootteja käytti 43% asukkaista ja 45% asukkaista käytti mielialalääkkeitä. Rauhoittavia lääkkeitä käytti säännöllisesti 26% ja unilääkkeitä 28% asukkaista. Dementiaa sairastavista asukkaista 11% käytti dementia-lääkitystä.

Yli puolet asukkaista (55%) käytti laksatiiveja säännöllisesti. Monimuuttuja-analyysissa niiden käyttöön liittyi korkea ikä, huono liikkumiskyky, huono ravitsemustila, puremisongelmat, Parkinsonin tauti ja suuri lääkemäärä. Välipalojen syönti liittyi vähäisempään laksatiivien käyttöön.

D-vitamiinivalmistetta käytti 33% ja kalsiumvalmistetta 28% asukkaista. Yhtäaikaaisesti D-vitamiini- ja kalsiumvalmistetta käytti 20% asukkaista. D-

vitamiiniannokset olivat pieniä: 21% asukkaista sai D-vitamiinia tutkimuksen aikaisen suositusannoksen 10µg (400 IU) ja 4% sai D-vitamiinia 20µg (800 IU) tai enemmän. D-vitamiinia käyttäneillä asukkailla oli parempi ravitsemustila, he söivät useammin välipaloja, heillä oli harvemmin ummetusta ja heidän painoaan seurattiin useammin kuin asukkailla, jotka eivät käyttäneet D-vitamiinivalmisteita.

Beersin vuoden 2003 kriteerien mukaan vanhuksille sopimattomia lääkkeitä käytti 34% asukkaista. Niiden käyttäjät käyttivät useammin psykielääläkkeitä ja yli yhdeksää lääketä päivittäin. He myös sairastivat harvemmin demetiaa kuin asukkaat, jotka eivät käyttäneet vanhuksille sopimattomia lääkkeitä. Yleisimmät sopimattomat lääkkeet olivat lyhytvaikutteiset bentsodiatsepiinit, joiden annostus oli suositusta suurempi, hydroksitsiini ja nitrofurantoiini. Näiden osuus kaikista vanhuksille sopimattomista lääkkeistä oli yhteensä lähes 77%. Lääkkeiden mahdolliselle yhteisvaikutukselle altistui alle 5% asukkaista. Keskeisimmät mahdollisiin yhteisvaikutuksiin liittyvät lääkkeet olivat kaliumia säästävät diureetit, karbamatsepiini ja kodeiini. Asukkaat, jotka altistuivat mahdolliselle lääkkeiden yhteisvaikutukselle olivat nuorempia, heillä oli useammin ollut aikaisempi aivoverenkiertohäiriö, he käyttivät useammin psykielääläkkeitä, vanhuksille sopimattomia lääkkeitä sekä yli yhdeksää lääketä päivittäin verrattuna lääkkeiden yhteisvaikutuksille altistumattomiin asukkaisiin. Ostopalveluvanhainkotien asukkaat käyttivät harvemmin yli yhdeksää lääketä päivittäin kuin julkisten vanhainkotien asukkaat.

Helsinkiläisten vanhainkotien pitkäaikaishoidossa olevat asukkaat käyttävät keskimäärin lähes kahdeksaa lääketä päivittäin. Psykielääläkkeiden käyttö on kansainvälisiin tutkimuksiin verrattuna erityisen yleistä. Laksatiivien käytön yleisyys ei eroa kansainvälisistä tutkimuksista. Vaikka D-vitamiinin hyödyt ovat tiedossa ja sen käytöstä on olemassa kansallinen suositus, yllättävän harvat vanhainkodin asukkaat saavat D-vitamiinia. Vanhuksille sopimattomien lääkkeiden käyttö on melko yleistä. Lääkkeiden yhteisvaikutukset eivät käytetyn mittarin valossa vaikuta olevan keskeinen ongelma vanhainkodeissa.

# 1 Introduction

Prescribing for older patients is challenging. The prevalence of diseases increases with advancing age and causes extensive drug use. Impairments in cognitive, sensory, social and physical functioning, multimorbidity and comorbidities, as well as age-related changes in pharmacokinetics and pharmacodynamics that impair the functional reserve of multiple systems and organs, all add to the complexity of prescribing. Consequently, older people are at particular risk for adverse drug events.

Drug therapy is an integral part of the care of older people. Optimizing drug prescribing for older adults is an important public health issue, especially in countries with a growing elderly population. Few randomized controlled trials include older multimorbid participants, and evidence-based guidelines recommending multiple drug regimens for the treatment of disorders common among older people are based on studies performed on younger individuals. In addition, the symptomatic relief of common conditions among older adults, such as pain and arthritis, increase the number of drugs used.

Interindividual variation in health, disease, and functional abilities increases with age and complicates decision-making in prescribing. Although the number of fit, healthy older people is rising, the number of older people with limited physiological reserve, reduced ability to recover from stress, dysregulation in immune and inflammation mechanisms, comorbidities and polypharmacy is also rising. The frailest older people, who are no longer capable of dwelling at home or in sheltered living, are admitted to nursing homes.

## 2 Review of the literature

### 2.1 Physiological changes in aging

Conventionally, the elderly have been defined most frequently by a chronological age of 65 years and older (Klotz 2009). However, the interindividual variability in health, disease, physiological responses, and disability – a phenomenon known as aged heterogeneity – increases substantially with aging, and the health status of the elderly varies more widely than does that of younger adults (Spinewine et al. 2007). Reduced homeostatic ability affects different regulatory systems in different individuals, which partly explains the increased interindividual variability (Mangoni & Jackson 2003).

Aging results from cumulative local effects at the molecular, cellular and tissue levels. Aging can be defined as a time-related loss of functional units, the disruption of regulatory processes providing functional integration between cells and organs, and failure to maintain homeostasis under physical stress (Mangoni & Jackson 2003). Primary aging is an inevitable, irreversible process in which the body slowly deteriorates with time (McLean & Le Couteur 2004). Secondary aging is a faster process resulting from illnesses and immobility. Secondary aging can be decelerated through lifestyle changes, physical activity, proper care, and rehabilitation. Aging results in anatomical and functional changes that may lead to the decompensation of a relevant system when the change progresses beyond a certain threshold (Mangoni & Jackson 2003). Progressive impairments in the functional reserve of multiple organs may increase the susceptibility of older people to stress as well as affect drug metabolism and pharmacokinetics (Klotz 2009).

#### 2.1.1 Pharmacokinetic and pharmacodynamic changes

Pharmacokinetics investigates drug absorption, distribution, metabolism, and excretion. Pharmacodynamics investigates drug effects and modes of action in the body. Aging affects both pharmacokinetics and pharmacodynamics.

##### *Pharmacokinetic changes in aging*

Aging affects gastric pH, gastrointestinal circulation, motility, and mucous membranes, but the overall effect in drug absorption from the intestines is clinically

insignificant (Turnheim 2004) (Table 1). Transdermal and subcutaneous absorption, as well as drug absorption from muscular tissue, may diminish due to reduced blood perfusion (Turnheim 2004). However, the evidence of age differences in percutaneous, transbronchial, and rectal routes of administration remains insufficient (Schwartz 2007).

The amount of metabolically active tissue decreases, and the relative amount of body fat increases; consequently, the lean body mass/body fat ratio decreases (Morley 1997). The distribution volume of hydrophilic drugs such as digoxin and furosemide decreases, and the use of diuretics may further reduce the amount of extracellular water (Turnheim 2004). The proportion of body fat and, consequently, the relative distribution volume of lipid-soluble drugs such as diazepam increases, thus prolonging their half-life and action (Turnheim 2004). The drug molecule-binding plasma albumin decreases, and the free fraction of the drug increases. After absorption, the blood circulation transports the drug molecules through the portal vein into the liver. The transformation of the drug molecules at this stage is known as first-pass metabolism.

The hepatic blood flow declines with aging, so drugs that the liver clears from the circulation display an age-dependent decrease in metabolic clearance (McLean & Le Couteur 2004). The activity of cytochrome P<sub>450</sub> enzymes, however, remains unaltered, at least in vitro, and in general, the interindividual variation in metabolic drug clearance by CYP enzymes exceeds the decline due to aging (Turnheim 2004).

An important pharmacokinetic change in aging is reduced renal function, glomerular filtration rate, tubular secretion, and renal blood flow (Mitchell et al. 2009). The decline in drug elimination may lead to elevated drug serum concentrations. Renal mass and the number of nephrons also decrease, and renal excretory function declines with advancing age in healthy individuals as well. Serum creatinine may remain within normal limits despite a reduction in creatinine clearance due to reduced muscle mass and creatinine production (Hutchison & O'Brien 2007). The Cockcroft-Gault equation (Cockcroft & Gault 1976) is the most widely used formula for estimating creatinine clearance (Hutchison & O'Brien 2007). The equation incorporates serum creatinine, age, gender, and weight to estimate creatinine clearance, and can thus serve to estimate creatinine clearance in older people in order to adjust the maintenance dose of renally excreted drugs with narrow therapeutic indices (Turnheim 2004). However, the Cockcroft-Gault equation underpredicts renal function for patients weighing less than their ideal body weight and overpredicts renal function for patients weighing more than their ideal body weight (Hutchison & O'Brien 2007).

**Table 1.** Age-related pharmacokinetic changes (adapted from Klotz 2009, Mangoni & Jackson 2003, Schwartz 2007, Mitchell et al. 2009, Hutchison & O'Brien 2007)

Age-related physiological change	Pharmacokinetic consequence
Gastric secretion ↓ Gastric emptying ↓ Splanchnic blood flow ↓ Absorption surface ↓ Gastrointestinal motility ↓  Body weight ↓ Body fat 25-30% ↑ Lean body mass 25-30% ↓ Plasma volume ↓ Extracellular body fluid ↓ Total body water 25-30% ↓  Serum albumin ↓  α1-acid glycoprotein ↑  Hepatic mass 20-40% ↓ Hepatic blood flow 20-50% ↓  Renal mass 20-30% ↓ Glomeruli 20-30% ↓ Renal blood flow ↓ Filtration fraction ↓ Tubular secretion ↓ Glomerular filtration rate 10% ↓ per decade	No clinically significant change in absorption  Increased volume of distribution, prolonged half-life, extended clearance of lipophilic drugs and elevated plasma concentration of hydrophilic drugs  Increased free fraction in plasma of a few highly protein-bound acidic drugs (e.g. warfarin)  Decreased free fraction in plasma of a few basic drugs (e.g. propranolol)  First-pass metabolism can be less effective, thus raising bioavailability. Some drugs may slightly impair phase I metabolism through the cytochrome P <sub>450</sub> enzyme system. No significant change occurred in phase II metabolism.  In the absence of disease, kidney function decreases less than previously thought. Aging can impair the renal clearance of drugs, which has a lower prevalence in women than in men.

### *Pharmacodynamic changes in aging*

Age-related changes in pharmacodynamics result in changes in the effector system: a decrease in the number of drug receptors, changes in receptor affinity, signal transduction, and end-organ response, as well as reduced counter-regulatory physiological and homeostatic processes that aim to preserve the original functional

equilibrium (Turnheim 2004, Mitchell et al. 2009, Hutchison & O'Brien 2007). Pharmacodynamic changes in old age include alterations in calcium channels, for example, and a reduction in the response of beta-adrenergic receptors, and heightened sensitivity to the sedating effects of certain medications as well as postural hypotension (McLean & Le Couteur 2004, Hilmer et al. 2007b) (Table 2). Risk for experiencing orthostatic hypotension increases due to reduced arterial compliance and baroreceptor reflex response (Hutchison & O'Brien 2007). Drugs that can exacerbate orthostatic hypotension include tricyclic antidepressants, antipsychotics, diuretics (especially loop diuretics), angiotensin-converting enzyme inhibitors, direct vasodilators, and opioids (Hutchison & O'Brien 2007). Other cardiovascular pharmacodynamic changes include increased risk for drug-induced QT interval prolongation and torsades de pointes, as well as the reduced number and responsiveness of muscarinic receptors (Hutchison & O'Brien 2007).

A decline in fluid and electrolyte homeostatic mechanisms exposes older people to adverse drug effects such as hyponatremia, inappropriate secretion of antidiuretic hormone, hyperkalemia, and dehydration (Hutchison & O'Brien 2007). Alterations in the number of neurons and receptors in the central nervous system, changes in the metabolism of neurotransmitters, and the greater permeability of the blood-brain barrier predispose the elderly to adverse drug reactions from central nervous system drugs. The elderly experience heightened sensitivity to benzodiazepines, which may cause ataxia, sedation and cognitive impairment, as well as to the anticholinergic effects of drugs (Hutchison & O'Brien 2007). The numbers of dopaminergic neurons and dopamine D2 receptors decrease with age, thus increasing the risk for extrapyramidal adverse drug reactions (Mitchell et al. 2009). Changes in patient medical status over time may cause long-term drug therapy to become unsafe or ineffective (Turnheim 2004).

### **2.1.2 Nutrition and aging**

Malnutrition results from insufficient intake of macronutrients (protein-energy malnutrition, vitamin and mineral deficiency), excessive intake of macronutrients (obesity), or excessive amounts of inappropriate substances such as alcohol (Omran & Morley 2000). The prevalence of undernutrition, often called malnutrition, among elderly home-dwellers is 1% to 15%, among the institutionalized elderly 21% to 60%, and among the hospitalized elderly 23% to 65% (Omran & Morley 2000, Guigoz 2006).

**Table 2.** Selected age-related pharmacodynamic changes (modified from Mangoni & Jackson 2003, McLean & Le Couteur 2004)

Drug	Pharmacodynamic effect	Age-related change
Adenosine	Heart-rate response	↔
Diazepam	Sedation, postural sway	↑
Diltiazem	Acute and chronic antihypertensive effect	↑
	PR-interval prolongation	↓
Diphenhydramine	Postural sway	↔
Enalapril	Angiotensin-converting enzyme inhibition	↔
Flunitrazepam	Sedation	↑
Furosemide	Peak diuretic response	↓
Heparin	Anticoagulant effect	↔
Isoprenaline	Chronotropic effect	↓
Midazolam	Sedation	↑
Morphine	Analgesic effect	↑
	Respiratory depression	↔
Phenylephrine	$\alpha_1$ -adrenergic responsiveness	↔
Propranolol	Antagonism of chronotropic effects of isoprenaline	↓
Salbutamol	Bronchodilatation	↓
Scopolamine	Cognitive function	↓
Temazepam	Postural sway	↑
Verapamil	Acute antihypertensive effect	↑
	PR-interval prolongation	↓
Warfarin	Anticoagulant effect	↑

One's energy expenditure and need for energy declines with advancing age, but one's need for nutrients is the same as or even greater than at a younger age (Russell 2000). Dryness of the mouth, as well as dental and swallowing problems, complicate chewing and swallowing, which may result in declining nutritional status (Soini et al. 2006). Illnesses, such as osteoarthritis and cardiovascular diseases, may



affect mobility, and decreasing mobility decreases appetite (Pitkälä & Strandberg 2003). Between the ages of 70 and 90, older people's energy intake declines by 20%, which accelerates the frailty process, sarcopenia and inflammation (Moreiras et al. 1996, Morley 2001, Wakimoto & Block 2001). With advancing age, one's sense of hunger and thirst weakens, which may, along with cognitive impairment, contribute to the onset of malnutrition (Naitoh & Burrell 1998). Reduced eating affects one's intake of beneficial nutrients, and the quality of one's diet becomes difficult to maintain (Ruiz-Lopez et al. 2003). Consequently, dietary guidelines for elderly people should emphasize nutrient-dense foods (Foote et al. 2000).

Aging reduces one's ability to regulate energy intake (Roberts & Rosenberg 2006). An older person experiencing energy deficit due to acute disease, for example, struggles to return to his or her preceding diet and to regain the lost weight (Roberts et al. 1994).

Malnutrition is especially common among nursing home residents (Saletti et al. 2000, Guigoz et al. 2002). The prevalence of malnutrition among institutionalized residents is about 21% to 40% (Guigoz 2006, Saletti et al. 2000, Suominen et al. 2005). Patients with dementia are at particularly high risk for malnutrition (Cronin-Stubbs et al. 1997). A Finnish study reported a daily energy intake of 1205 and 1230 kcal among 44 female residents in dementia wards, which represents only 66% to 77% of the recommended daily energy intake for females aged  $\geq 75$  years (Suominen 2007). The Finnish National Nutrition Council has published its first guidelines for the nutrition and nutritional care of older people in March 2010 (Suominen et al. 2010).

Nutritional status significantly affects drug metabolism (Turnheim 2004). Advanced malnutrition may lower the plasma albumin concentration, which raises the concentration of free drug molecules in circulation, and thus may fortify the effect of the drug (Javaid & Morley 2000). Dehydration, loss of total body water, and decrease of lean body mass may lead to a higher concentration of water-soluble drugs and a longer half-life of lipid-soluble drugs (Javaid & Morley 2000). On the other hand, drugs can also affect appetite and nutrition. Drugs with anticholinergic properties can cause dryness of the mouth and slow gastrointestinal peristalsis. Constipation-inducing drugs, such as opioids, can affect appetite, and thus increase the risk for malnutrition. Some drugs, such as anticholinesterases (AChEs), selective serotonin reuptake inhibitors (SSRIs) and macrolides, may cause diarrhea and nausea (Pharmaca Fennica 2010), thus increasing the risk for poor appetite and malnutrition.

## *Assessment of nutritional status*

Good nutritional status in old age contributes to health and the ability to recover from illness. Early detection of malnutrition and the risk for undernutrition are essential for improving the care of older people (Reynish & Vellas 2001). The full assessment of elderly people's nutritional status includes several biochemical and anthropometric measurements, but performing a full assessment for all nursing home residents is neither practical nor cost-effective (Reynish & Vellas 2001). Screening for nutritional status is a rapid and simple process performed by health care teams, whereas a full nutritional assessment is a detailed examination that involves several measures ranging from subjective assessment to objective measurements of metabolic, nutritional or functional variables performed by an expert clinician, nutrition nurse or dietician (Green & Watson 2006, Kondrup et al. 2003). Regular weight monitoring should be implemented as a surveillance measure of nutritional status (Cowan et al. 2004), and all patients should be screened on admission to hospitals or other institutions (Kondrup et al. 2003).

A meta-analysis taking into account 21 different nutritional screening and assessment tools for older adults, proved that the Mini Nutritional Assessment (MNA), was the most extensively evaluated tool for screening the nutritional status of the frail elderly (Green & Watson 2006). MNA is reliable and well validated, involves no laboratory analyses, and is suitable for screening large populations (Omran & Morley 2000, Guigoz 2006, Guigoz et al. 2002). MNA includes 18 variables: anthropometric measurements (BMI, weight loss, arm and calf circumferences), general health assessment (dwelling place, medication, mobility, acute disease or stress, signs of depression or dementia, skin ulcers), short dietary assessment (number of meals, protein, vegetable and fluid intake, mode of feeding), and subjective assessment (self perception of health and nutrition) (Vellas et al. 1999 and 2006). Nutritional status is assessed in two steps. The MNA short form serves to screen nutritional status, and if a concern about possible malnutrition arises, the complete version of MNA follows. MNA takes less than 15 minutes to complete. The complete version of MNA provides a maximum of 30 points and distinguishes individuals as having adequate nutritional status ( $\geq 24$  points), at risk for malnutrition (17-23.5 points), and protein-calorie malnutrition ( $< 17$  points) (Vellas et al. 1999). Usually, patients with a score of 17.5 to 23.5 points have not yet begun to lose weight and show no low plasma albumin levels, but often have a lower protein-calorie intake than recommended (Vellas et al. 2006). MNA is likely to detect the risk for and early stages of undernutrition, since the method assesses physical and mental aspects of health that often affect the nutritional status of the elderly (Kondrup et al. 2003).

## 2.2 Drug use among the elderly

### 2.2.1 Epidemiology of drug use

Elderly people have multiple morbidities and symptoms, and thus use a considerable number of medications. Two thirds of people aged  $\geq 65$  years and over 90% of people aged  $\geq 80$  years take medications regularly (Giron et al. 1999).

In Lieto, a municipality in south-western Finland, 78% of the home-dwelling elderly aged  $\geq 64$  years used at least one prescription drug in 1990-1991; in 1998-1999, this figure rose to 88% (Linjakumpu et al. 2002a). The mean number of prescription medications rose from 3.1 to 3.8 (Linjakumpu et al. 2002b). In Kuopio, a city in eastern Finland, 90% of those aged  $\geq 75$  years used regular medication in 1998 and 97% in 2003 (Jyrkka et al. 2006). In both samples, people living in institutions took significantly more medication regularly and as needed than did community-dwellers: the numbers of medications institutionalized people took were 4.7 (regularly) and 2.8 (as needed) in 1998, and 7.2 (regularly) and 3.7 (as needed) in 2003. Among community-dwellers, the figures were 4.0 (regularly) and 2.3 (as needed) in 1998, and 5.4 (regularly) and 1.7 (as needed) in 2003 (Jyrkka et al. 2006).

In the US, people aged 65 or older (12% of the population) are prescribed one third of all drugs and consume more than half of all over-the-counter medications (Ostrom et al. 1985). Home-dwelling older people consume on average four to five medications (Giron et al. 1999), whereas those dwelling in nursing homes and geriatric wards consume on average eight to ten medications (Pitkala et al. 2004, Socialstyrelsen 2004). Information about drug use among the home-dwelling elderly may be less reliable than among institutionalized older people. In Finland, register data are available only for prescription medications, not for over-the-counter drugs. Moreover, whether or how a home-dweller actually consumes the medications remains uncertain.

### 2.2.2 Psychotropic medication

#### *Epidemiology of psychotropic medication use*

Psychotropic drugs are classified as antipsychotics (N05A), antidepressants (N06A), anxiolytics (N05B), hypnotics (N05C), and anti-dementia drugs (N06D) (ATC DDD 2009). The use of these medications is very common among the elderly.

In Lieto, the prevalence of psychotropic drugs among the home-dwelling elderly aged  $\geq 64$  years was 24% in 1990-1991 and 27% in 1998-1999 (Linjakumpu et al. 2002a). In both samples, hypnotics/sedatives were the most prevalent psychotropic drugs (Linjakumpu et al. 2002a). In the Swedish Kungsholmen project, which comprised Stockholm-dwelling elderly aged  $\geq 81$  years, the institutionalized participants used more psychotropic drugs than did the non-institutionalized in 1987-1989 (60.3% vs. 38.5%) and in 1994-1996 (71.1% vs. 36.2%) (Giron et al. 2001).

The Minimum Data Set, a standardized, clinically based assessment instrument that collects information on each nursing home resident's demographic, functional, medical, psychological, and cognitive status (Liperoti et al. 2003), has provided some information on psychotropic drug use in nursing homes in Finland (Noro et al. 2005). Studies reporting the prevalence of psychotropic drug use among nursing home residents are listed in Table 3.

### *Indications of psychotropic medications among the elderly*

Dementia, with its psychological and behavioral symptoms, is the most common reason for admittance to institutional care (Phillips & Diwan 2003). Antipsychotics often serve to treat psychotic symptoms as well as to control the behavioral and psychological symptoms of dementia (Avorn & Gurwitz 1995).

The Nursing Home Reform Act, embedded within the Omnibus Budget Reconciliation Act 1987 (OBRA 87), was enacted to restrict psychotropic drug use in long-term care in the US (McGrath & Jackson 1996, Snowden & Roy-Byrne 1998, Hughes & Lapane 2005). This legislation states that each resident's drug regimen must not include unnecessary drugs (defined as drugs used in excess dose or duration, or without adequate monitoring or indication) or adverse reactions that suggest the drug should be discontinued or the dosage lowered (Hughes & Lapane 2005).

The OBRA 87 states that residents have the right to be free of psychotropics administered without proper indication. Disallowed indications for antipsychotic drug use include wandering, restlessness, anxiety, and uncooperativeness. Antipsychotic drug use is permitted if the patient has schizophrenia, schizoaffective disorder, or delusional disorder.

According to the OBRA 87, a consultant pharmacist should evaluate a patient's drug regimen on a monthly or quarterly basis (Hughes & Lapane 2005). In 1999, the Beers criteria for potentially inappropriate medication use and a set of quality indicators were incorporated within the OBRA 87 (Hughes & Lapane 2005). In 2004, 5 of the 24 quality indicators were related to psychotropic drug use: i) the prevalence of

**Table 3.** Studies describing the use of psychotropic drugs in nursing homes

Study	Country	N	Any psychotropic %	Antipsychotics %	Antidepressants %	Anxiolytics %	Hypnotics %
Snowdon et al. 1995	Australia	2414	59	27	16	9	27
McGrath & Jackson 1996	UK	909		24			
Llorente et al. 1998	USA	1573		18			
Lasser & Sunderland 1998	USA	298	70	42	61	41	
Snowdon 1999	Australia	1975	49	23	16	6	17
van Dijk et al. 2000	Netherlands	2355	74	35	17	28	54
Ruths et al. 2001	Norway	1552	59	23	31	15	14
Sorensen et al. 2001	Denmark	288	56	21	24	38	
Nilsson & Petersson 2001	Sweden	405	59	21	33	17	30
Draper et al. 2001	Australia	647	52	22	20	9	23
Ford et al. 2002	UK	125 (1999) 119 (2001)		38 37			
Oborne et al. 2002	UK	934		25			
Liperoti et al. 2003	USA	139714		15			
Mamun et al. 2003	Singapore	384		24	28		
Holmquist et al. 2003	Sweden	175	73	16	33	32	45
Nygaard et al. 2004	Norway	1247 (1985) 1035 (1996-7)	52 57	33 22	12 31	11 16	11 14

**Table 3 continued.** Studies describing the use of psychotropic drugs in nursing homes

Study	Country	N	Any psychotropic %	Antipsychotics %	Antidepressants %	Anxiolytics %	Hypnotics %
Gobert & D'hoore 2005	Switzerland	7592	78				
	Canada	8183	67				
Snowdon et al. 2005	Australia	2302		25			
Snowdon et al. 2005	Australia	3093	47		21	4	11
Alanen et al. 2006	Finland	1334 (≥ 90 yrs)		30	34	26	34
	Norway	933 (with dementia)	75	26	39	24	26
Meyer et al. 2008	Germany	2367	52	28	20		
Nijk et al. 2009	Netherlands	1322 (with dementia)	63				
	Australia	1844	75	46	37	22	13

antipsychotic use in the absence of psychotic or related conditions, ii) the prevalence of any anxiolytic/hypnotic use, iii) the prevalence of hypnotic use more than twice in the past week, iv) the prevalence of symptoms of depression, and v) the prevalence of depression with no antidepressants.

The psychotropic drug administrative initiative has reduced antipsychotic prescribing in the US (Hughes & Lapane 2005). Finnish authors suggest evaluating an older patient's drug regimen when necessary and at least once a year (Hartikainen & Seppälä 2007).

### **2.2.3 Laxatives**

Constipation is one of the most common complaints among the frail elderly. More than half of nursing home residents have constipation (Phillips et al. 2001). The Rome III consensus criteria define functional constipation as a functional bowel disorder with persistently difficult, infrequent, or seemingly incomplete defecation which does not meet irritable bowel syndrome criteria (Longstreth et al. 2006). Patients complaining of constipation may suffer from colonic inertia or anorectal dyssynergia, but most patients experience normal colonic transit and anorectal function (Longstreth et al. 2006). Even though the incidence of constipation increases with age, healthy elderly do not necessarily suffer from constipation, and constipation should not be considered unavoidable due to advancing age.

Constipation is the only indication for laxatives; consequently, they may serve as a marker for constipation (van Dijk et al. 1998, Harari et al. 1995, Monane et al. 1993). Laxative consumption increases with age, and 50% to 74% of nursing home residents regularly receive laxatives (van Dijk et al. 2000, Phillips et al. 2001, van Dijk et al. 1998, Harari et al. 1995, Monane et al. 1993, Brocklehurst et al. 1999, Kinnunen 1991). Despite their extensive use, a meta-analysis reported insufficient evidence of the efficacy of laxatives over placebo in chronic constipation due to lack of published research (Jones et al. 2002). In addition, many consider the long-term use of some bowel-stimulating laxatives inappropriate for the elderly (Fick et al. 2003).

Studies on older nursing home residents have reported a significant association between constipation and Caucasian ethnicity, low fluid intake, pneumonia, Parkinson's disease, allergies, immobility, arthritis, polypharmacy, new medications, dementia, hypothyroidism, and hypertension (Robson et al. 2000) as well as between laxative use and immobility, Parkinson's disease, and diabetes mellitus (Harari et al. 1995). In testing the effectiveness of a particular medication, numerous clinical drug trials have reported constipation as a side effect. Even so, large-scale epidemiological

studies describing the associations of drugs and constipation are nevertheless scarce. Studies on older nursing home residents have shown that iron supplements (van Dijk et al. 1998, Harari et al. 1995), calcium channel blockers (Harari et al. 1995), verapamil (van Dijk et al. 1998), calcium supplements (van Dijk et al. 1998), anticholinergic neuroleptics (Monane et al. 1993), and anticholinergic antidepressants (Harari et al. 1995, Monane et al. 1993) are associated with laxative use.

Nurses play a significant role in the assessment and treatment of constipation. The staffing costs account for 70% of total drug costs in constipation care (Pekmezaris et al. 2003).

#### **2.2.4 Vitamin D and calcium**

Fractures in the elderly are associated with two risk factors: the loss of bone mass due to osteoporosis and increased susceptibility to falls (Meunier et al. 1994, Boonen et al. 2006). The annual rate of falling among home-dwelling people aged  $\geq 65$  years is 0.3 to 1.6 per person; 5% of these falls induce a fracture or require hospitalization (Rubenstein 2006). For nursing home-dwellers, the annual rate is much higher: 0.6 to 3.6 per bed; 10% to 25% of the falls result in fracture or laceration (Rubenstein 2006).

A growing body of evidence shows that vitamin D and calcium play a role in preventing falls and fractures (Meunier et al. 1994, Bischoff-Ferrari et al. 2005, Bischoff-Ferrari et al. 2004a, Bischoff-Ferrari et al. 2004b). Vitamin D and calcium benefit calcium homeostasis and bone mineral density, and vitamin D improves musculoskeletal function, thus reducing the risk from falls (Boonen et al. 2006, Bischoff-Ferrari et al. 2004b).

Vitamin D is a derivate of cholesterol. Cholecalciferol (vitamin D<sub>3</sub>) is synthesized in the skin in a photochemical reaction driven by ultraviolet radiation. Ergocalciferol (vitamin D<sub>2</sub>) is of vegetable origin. Both vitamin D<sub>3</sub> and D<sub>2</sub> can be obtained from food and vitamin supplements. Ergocalciferol and cholecalciferol are inactive; they must be first hydrolyzed into 25-hydroxycholecalciferol in the liver and then into the active 1,25-dihydroxycholecalciferol in the kidneys (Pelkonen & Ruskoaho 2003).

In both active and inactive ambulatory persons aged  $\geq 60$  years, serum 25-hydroxycholecalciferol concentrations of 40 to 90 nmol/l were associated with better musculoskeletal function in the lower extremities than were concentrations of  $< 40$  nmol/l (Bischoff-Ferrari et al. 2004b). Calcium absorption seems to be maximized in serum 25-hydroxycholecalciferol concentrations of  $> 80$  nmol/l (Heaney 2004). In a US study of healthy adult men, the mean serum 25-hydroxycholecalciferol



concentration in autumn was 70 nmol/l. The dose of vitamin D supplementation needed to sustain this serum 25-hydroxycholecalciferol concentration during wintertime was 500 IU (12.5 µg) daily (Heaney et al. 2003). Elderly people who live in the northern latitudes and in institutions, and thus spend much of their days indoors, are at particular risk for low serum 25-hydroxycholecalciferol concentrations. In addition, even in the presence of solar radiation, the cutaneous intake of cholecalciferol decreases with age (Heaney 2004).

A meta-analysis of 12 trials found that oral cholecalciferol (vitamin D3) in a daily dose of 700-800 IU (17.5-20 µg) or intermittent doses of 100 000 IU (2500 µg) every four months, with or without calcium, significantly reduced both hip and non-vertebral fractures (Bischoff-Ferrari et al. 2005). No significant benefit was observed for a daily dose of 400 IU (10 µg) of oral cholecalciferol (Bischoff-Ferrari et al. 2005); other studies confirm these findings (Bischoff-Ferrari & Dawson-Hughes 2007, Venning 2005, Broe et al. 2007). In a meta-analysis of five randomized controlled trials involving 1237 elderly participants, vitamin D in a daily dose of 800 IU (20 µg) or more reduced falling by 22% compared with patients receiving calcium or placebo; the number treated was 15 (Bischoff-Ferrari et al. 2004a).

UV light exposure, food fortification, and supplements can contribute to the prevention of vitamin D deficiency. Vitamin D and calcium are an integral part of treatment for patients with osteoporosis, and are recommended for all elderly living in institutions. Vitamin D and calcium supplements are useful for older people at risk for low calcium intake, lacking exposure to sunlight, with low femoral bone density, a high serum parathyroid hormone concentration, a low serum 25-hydroxyvitamin D concentration, and a previous history of falls (Meunier et al. 1994). In the US, 32% of female nursing home residents received vitamin D supplements (Gupta & Aronow 2003). In another US study, vitamin D was administered to 9% of nursing home residents, and calcium to 12% (Kamel 2004).

The Finnish National Nutrition Council updated its recommendations concerning vitamin D intake in March 2010. They currently recommend supplementation in a daily dose of 800 IU (20µg) for older and institutionalized people (Suominen et al. 2010). The former recommendation was daily dose of 400 IU (10 µg). The Finnish Current Care Guideline for osteoporosis recommends vitamin D in a daily dose of 700 to 800 IU (17.5-20 µg) along with a calcium supplement (Current Care Guidelines).

## 2.3 Appropriate and inappropriate prescribing

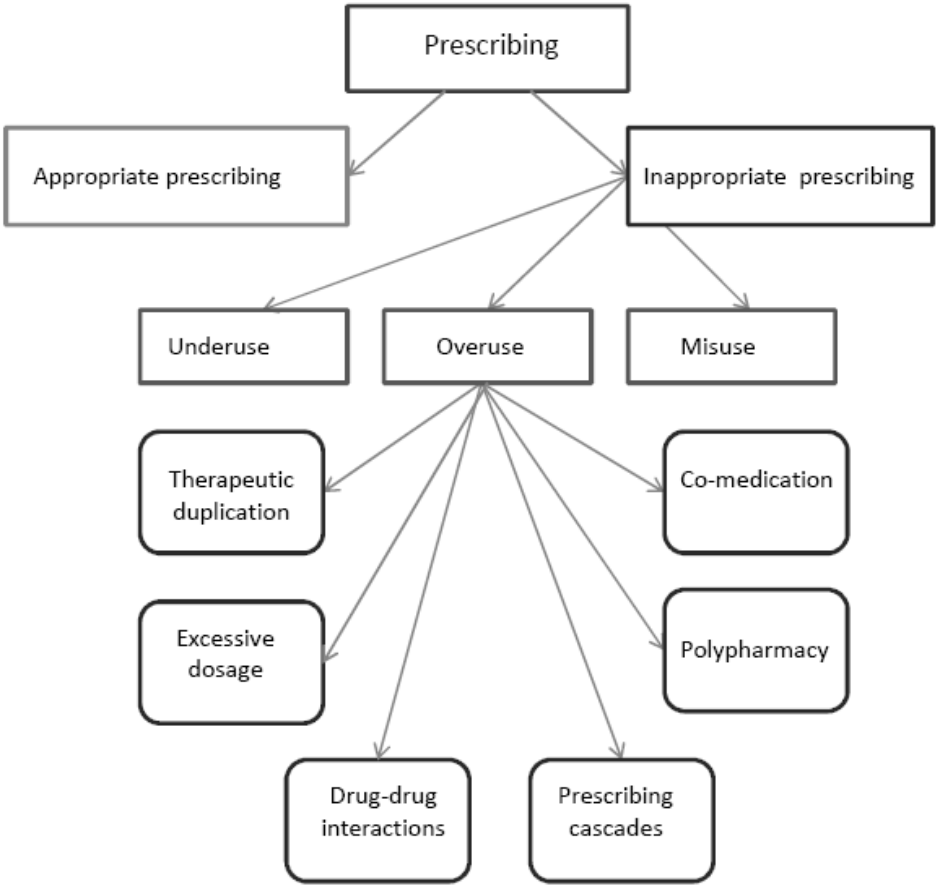
Quality of care, including prescribing, can be defined as the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge (Lohr & Schroeder 1990).

The Oxford English Dictionary defines appropriate as suitable or proper to or for a particular purpose. Buetow et al. suggest that appropriate prescribing is an outcome of a process of decision-making that maximizes net individual health gains within society's available resources (Buetow et al. 1997). They wish to differentiate the rationale of prescribing from the appropriateness of prescribing, and suggest that rationalism of prescribing refers to the prescribing process and appropriateness to its outcome. Thus, prescribing may be rational, but inappropriate when correct reasoning leads to a poor outcome due to, for example, inadequate information or communication problems. Moreover, the prescribing process may be irrational, but lead to an appropriate outcome (Buetow et al. 1997). The authors suggest that the suitable allocation of resources is a prerequisite of appropriate prescribing, and the objective is a balance between maximizing patient welfare and distributing resources according to need (Buetow et al. 1997). More simply, appropriate prescribing implies that the quality of prescribing is what should be achieved in practice (Spinewine et al. 2007). The appropriateness of prescribing can also be assessed with following criteria: i) what the patient wants; ii) scientific rationalism, including clinical pharmacology of the drug; and iii) the general good (Spinewine et al. 2007).

Health care quality problems, including prescribing quality problems, may be classified as underuse, overuse, and misuse (Chassin & Galvin 1998) (Figure 1). Underuse is a failure to provide a service, in this case a medication, when it would have produced a favorable outcome for a patient. Overuse is providing a medication under circumstances in which the potential for harm exceeds the potential benefit. Misuse is selecting an appropriate medication, but prescribing it inappropriately (Chassin & Galvin 1998).

Inappropriate prescribing can cause substantial morbidity and represents a clinical and economic burden to patients and society (Gurwitz et al. 1990, Hanlon et al. 2001); inappropriate prescribing in elderly people has therefore become an essential public health issue worldwide (Spinewine et al. 2007). Reducing overuse and misuse improves the quality of care by sparing patients unnecessary risk and complications and reducing costs. Although solving underuse problems improves quality, it may increase costs (Chassin & Galvin 1998). Whether the costs actually rise, however, depends on the intervention and the time scale.

Evidence-based treatment of multimorbidities necessitates the use of multiple drugs; however, age-related factors predispose patients to adverse drug effects (ADEs) as well as to drug-drug interactions (DDIs). Among nursing home residents, impairments in cognitive, sensory, social and physical functioning, comorbidities, and age-related changes in pharmacokinetics and pharmacodynamics all contribute to the complexity of prescribing.



**Figure 1.** Terminology of prescribing (adapted from Chassin & Galvin 1998 and Hemminki & Turakka 1977).

**2.3.1 Polypharmacy**

Polypharmacy is commonly defined as the use of multiple medications or the use of a medication for which there is no indication (Bushardt et al. 2008). In US nursing homes, the suggested criterion for polypharmacy is the daily consumption of  $\geq 9$

drugs (Hanlon et al. 2001). Other definitions in current use include minor polypharmacy (2-4 drugs daily) and major polypharmacy ( $\geq 5$  drugs daily) (Bjerrum et al. 1997, Thomas et al. 1999), as well as excessive polypharmacy ( $\geq 10$  drugs daily) (Jyrkka et al. 2006 and 2009). Some studies define polypharmacy as the long-term use of two or more medications for at least 60 days per three-month period (Veehof et al. 1999 and 2000). Polymedicine means the use of multiple medications for the treatment of multiple comorbid conditions (Monane et al. 1997).

Risk factors for polypharmacy include old age, comorbidity, poor self-rated health, recent hospitalization, female gender, low educational attainment, depression, multiple prescribers and prescriber characteristics (Linjakumpu et al. 2002b, Thomas et al. 1999, Jyrkka et al. 2009, Haider et al. 2009). In a study on polypharmacy among men aged 56-75 years in South Wales, 9% of the participants used  $\geq 5$  drugs per day; factors associated with the use of  $\geq 5$  drugs included increasing age, lower social class, unemployment, smoking, and obesity (Thomas et al. 1999). In Lieto, the use of  $\geq 5$  drugs daily among the home-dwelling elderly rose from 19% in 1990-1991 to 25% in 1998-1999 (Linjakumpu et al. 2002b). In the Kuopio 75+ cross-sectional study of the home-dwelling elderly, the factors associated with the use of  $\geq 10$  drugs daily (including regular and as-needed medications) were age  $\geq 85$  years, female gender, moderate or poor self-reported health, diabetes mellitus, depression, pain, heart disease, and obstructive pulmonary disease (Jyrkka et al. 2009). In a prospective Kuopio 75+ study, which also included the institutionalized participants, the prevalence of participants consuming  $\geq 5$  drugs daily rose from 54% in 1998 to 67% in 2003, and the prevalence of participants consuming  $\geq 10$  drugs daily rose from 19% in 1998 to 28% in 2003 (Jyrkka et al. 2006).

Most clinical care guidelines fail to take into account multimorbidities, and strict adherence to guidelines in prescribing for older patients with multiple comorbidities may result in polypharmacy (Boyd et al. 2005) and thus diminish the quality of care among the elderly. The possible harmful effects of polypharmacy include adverse drug effects, drug-drug interactions, higher costs, poor patient compliance with medication administration, higher incidence of nursing home placement, errors in the administration of drugs, and the unintentional prescribing of additional drugs for the adverse effects of other drugs, also known as the prescribing cascade (Hilmer et al. 2007b, Thomas et al. 1999, Satish et al. 1996).

Some views support the use of multiple drugs. Several studies show that the elderly need drugs including preventive medications and benefit from them, but often go undertreated (Gurwitz 2004, Sloane et al. 2004, Rochon & Gurwitz 1995 and 1999, Ebrahim 2002). Some authors have suggested that the intention to reduce the use of

drugs among the elderly should not be the only aim in treatment, and polypharmacy may prove beneficial in controlling many diseases among the elderly (Gurwitz 2004, Rochon & Gurwitz 1995). In many diseases, the use of multiple drugs in treatment has proved more effective than using only one or two drugs (Gurwitz 2004).

### **2.3.2 Potentially inappropriate drugs in the elderly**

In 1991, Beers et al. published explicit criteria regarding potentially inappropriate drugs (PIDs) among older nursing home residents (Beers et al. 1991). The criteria were created by a US panel of experts in geriatric care, clinical pharmacology, and psychopharmacology using a modified Delphi technique to reach consensus. The criteria were updated in 1997 for all older people (Beers 1997), and the latest version was published in 2003 (Fick et al. 2003) (Table 4). These criteria consider a drug inappropriate for older adults if evidence of its efficacy is insufficient, if the potential adverse drug effects outweigh the benefits, or if a safer alternative exists. The latest versions also include criteria for drugs that should be avoided in older adults with certain diagnoses or conditions (i.e. drug-disease interactions). The Beers criteria have been more widely used than other criteria (McLeod et al. 1997, Naugler et al. 2000) to describe inappropriate prescribing in older adults, although difficulties in generalizing explicit criteria from one country to another do exist (Spinewine et al. 2007).

The prevalence of PIDs among elderly home-dwellers in Helsinki was 13% in 1998-1999 (Pitkala et al. 2002). The most common PIDs in this population include dipyridamole, long-acting benzodiazepines, amitriptyline, ergot mesyloids, muscle relaxants, and meprobamate. Moreover, the use of drugs considered inappropriate with regard to certain diagnoses or conditions was common (Pitkala et al. 2002).

In a US study of nearly 17 000 community-dwelling elderly, 41% received one PID (according to the Beers 2003 criteria), and 14% received two or more PIDs (Fick et al. 2008). The most common PIDs in this population included estrogen, propoxyphene, and short-acting benzodiazepine in greater doses than recommended (Fick et al. 2008).

A multicenter study that included eight countries across Europe combined the Beers 1997 and 2003 criteria and the McLeod criteria to assess PID use among elderly home care patients (Fialova et al. 2005). Of all the 2707 participants, 20% used at least one PID (according to the combined criteria), ranging from 6% in Denmark to 41% in the Czech Republic.

**Table 4.** PIDs independent of diagnoses and conditions (modified from Fick et al. 2003)

Potentially inappropriate drug	Concern
A02BA01 <i>cimetidine</i>	Central nervous system ADRs including confusion
Gastrointestinal antispasmodic drugs: A03AA07 <i>dicyclomine (dicycloverine)</i> , A03BA03 hyoscyamine, A03AB05 <i>propantheline</i> , A03B belladonna alkaloids, A03CA02 clidinium-chlordiazepoxide	Anticholinergic ADRs, uncertain effectiveness
A04 <i>trimethobenzamide</i>	Ineffective, extrapyramidal ADRs
A06AA01 <i>mineral oil</i>	Aspiration, ADRs
Stimulant laxatives in long-term use without the co-administration of opiates: A06AB02 bisacodyl A06AB07 <i>cascara sagrada</i> A06AB05 <i>castor oil</i>	Bowel dysfunction
A10BB02 <i>chlorpropamide</i>	Prolonged hypoglycemia
B01AC05 <i>ticlopidine</i>	No better than acetylsalicylic acid, but more toxic
B01AC07 short-acting dipyridamole	Orthostatic hypotension
B03AA07 ferrous sulphate > 325 mg/day	Constipation in high doses
C01AA05 digoxin > 0.125 mg/day (except when treating atrial arrhythmias)	Reduced renal clearance may lead to higher risk for toxic effects
C01BA03 disopyramide	Negative inotrope, heart failure, anticholinergic ADRs
C01BD01 amiodarone	QT interval problems, torsades de pointes, ineffective
C02AA02 <i>reserpine</i> > 0.25 mg C02AB <i>methyldopa and comb.</i>	Depression, impotence, sedation, orthostatic hypotension Bradycardia, may exacerbate depression
C02AC01 clonidine	Orthostatic hypotension, central nervous system ADRs
C02CA04 <i>doxazosin</i>	Hypotension, dry mouth, urinary problems
C02CC02 <i>guanethidine, guanadrel</i>	Orthostatic hypotension
C03CC01 <i>etacrynic acid</i>	Hypotension, fluid imbalances
C04AA01 <i>isoxsuprine</i> C04AE01 ergot mesyloids C04AX01 cyclandelate	Uncertain or lack of efficacy
C08CA05 short-acting nifedipine	Hypotension, constipation
G03BA02 methyltestosterone G03C estrogens only (oral)	Prostatic hypertrophy, cardiac problems Carcinogenic potential, lack of cardio protective effect
H03AA05 <i>desiccated thyroid</i>	Cardiac effects
J01XE01 nitrofurantoin	Renal impairment
M01AB01 indomethacin	Central nervous system ADRs

**Table 4. continued** PIDs independent of diagnoses and conditions

Potentially inappropriate drug	Concern
M01AB15 ketorolac	Avoid because of elderly people's asymptomatic pathological gastrointestinal conditions
Non-selective longer half-life NSAIDs in long-term, full-dosage use:	Gastrointestinal bleeding, renal and heart failure, hypertension
M01AE02 naproxen	
M01AE12 <i>oxaprozin</i>	
M01AC01 piroxicam	
Muscle relaxants and antispasmodics:	Anticholinergic ADRs, effectiveness questionable
M03BA03 <i>methocarbamol</i>	
M03BA02 <i>carisoprodol</i>	
M03BB03 <i>chlorzoxazone</i>	
M03BB <i>metaxalone</i>	
M03BX08 <i>cyclobenzaprine</i>	
G04BD04 short-acting oxybutynin	
N02AB02 meperidine (pethidine)	Ineffective, causes confusion
N02AC04 propoxyphene and comb.	Few advantages over paracetamol, ADRs of other narcotic drugs
N02AD01 <i>pentazocine</i>	CNS ADRs
N03AA barbiturates (except for seizures)	Addictive, cause more ADRs than most sedative or hypnotic drugs
N04AB02 orphenadrine	Sedation and anticholinergic ADRs
N05AC02 thioridazine	Central nervous system and extrapyramidal ADRs
N05AC03 <i>mesoridazine</i>	
N05BC01 meprobamate	Highly addictive, sedation
Long-acting benzodiazepines:	Sedation, risk for falls and fractures
N05BA02 chlordiazepoxide	
N05BA01 diazepam	
N05CD10 <i>quazepam</i>	
N05BA13 <i>halazepam</i>	
N05BA05 <i>chlorazepate</i>	
Short-acting benzodiazepines in high doses:	Smaller doses effective and safer
N05BA06 lorazepam > 3 mg	
N05BA04 oxazepam > 60 mg	
N05BA12 alprazolam > 2 mg	
N05CD07 temazepam > 15 mg	
N05CD05 triazolam > 0.25 mg	
N05CD01 <i>flurazepam</i>	Extremely long half-life
N06AA09 amitriptyline and comb.	Anticholinergic ADRs
N06AA12 doxepin	

**Table 4. continued** PIDs independent of diagnoses and conditions

Potentially inappropriate drug	Concern
N06AB03 fluoxetine daily	CNS stimulation, sleep disturbances, increasing agitation
N06BA01-03 <i>amphetamines</i>	CNS stimulation ADRs
Anticholinergics and antihistamines:	Anticholinergic ADRs
R06AB02 <i>chlorpheniramine</i>	
R06AA02 diphenhydramine	
N05BB01 hydroxyzine	
R06AX02 <i>cypheptadine</i>	
R06AD02 <i>promethazine</i>	
R06AC04 tripeleminamine	
R06AB02 <i>dexchlorpheniramine</i>	

PIDs unavailable in Finland in 2003 are marked in *italics*.

The code preceding the drug name refers to the ATC code.

According to the Beers 2003 criteria, approximately 17% of all participants were PID users, ranging from 7% in Denmark to 25% in the Czech Republic. The PIDs most commonly used were pentoxifylline and diazepam. The most common PIDs (prevalence  $\geq 3\%$ ) in Czech Republic were pentoxifylline, diazepam, and amiodarone; diazepam and amitriptyline in Finland; unopposed estrogens in Iceland; amiodarone and ticlopidine in Italy; diazepam in the Netherlands and Norway; and amiodarone in the United Kingdom (Fialova et al. 2005).

The use of PIDs is also common in nursing homes (Table 5). Factors associated with inappropriate prescribing among the elderly have included female gender, age, polypharmacy, poor physical functioning, no diagnosis of dementia, and several prescribers (Fick et al. 2008, Dhall et al. 2002, Dhalla et al. 2002). About one third of the nursing homes in Finland participate in benchmarking by using the Minimum Data Set (Noro et al. 2005, Morris et al. 1990), which also includes certain quality indicators for drug prescribing.

## 2.4 Drug-drug interactions

Drug interactions can be categorized into interactions between i) two or more drugs, ii) drug and disease or condition, iii) drug and food products, iv) drug and alcohol, and v) drug and natural products, such as herbs (Mallet et al. 2007). Figure 2 introduces drug-drug interactions.



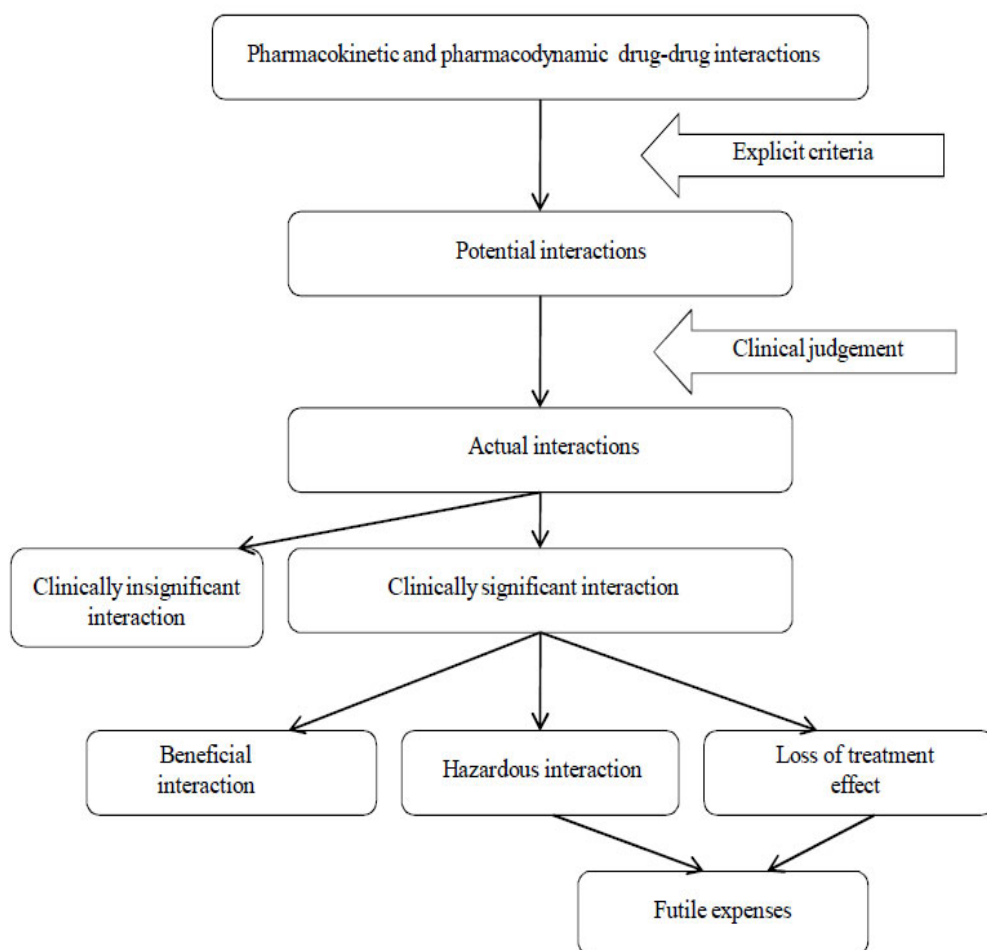
**Table 5.** PID use in nursing homes according to the Beers criteria

Study	N	Users of PIDs	The most prevalent PIDs	Factors associated with PID use
Beers et al. 1992	1106	40.3%*	Iron supplements in greater doses than recommended, long-acting benzodiazepines, persantine, propoxyphene	Female gender, a large NH
Gupta et al. 1996 (PID exposure during 1 year)	19 932	48.8*		
Dhalla et al. 2002 (1 year after admission)	1991	20.8% **	Strongly anticholinergic antidepressants, long-acting benzodiazepines, oxybutynine	Age ≤ 85 years, several prescribers, prescriber characteristics
Dhall et al. 2002 (90 days after admission)	2908 2	31 %**	Propoxyphene, hydroxyzine, diphenhydramine, digoxin, iron supplement in greater doses than recommended	Female gender, ≥ 9 drugs daily, admission from hospital, no cognitive impairment, poor physical functioning
Nygaard et al. 2003	1042	25.3%**	Flunitrazepam and nitrazepam, inappropriate antihistamines, inappropriate antipsychotics	Number of drugs, DDIs, no mental impairment
Lane et al. 2004	5871 9	2.3%	Diazepam	
Lau et al. 2004 (PID exposure during 1 year)	3372	49.7% **,***	Propoxyphene, diphenhydramine, hydroxyzine, oxybutynine, amitriptyline, cyproheptadine, iron and ranitidine in greater doses than recommended	Medicaid coverage, nondementia mental disorder, no communication problems, number of drugs, a non-accredited NH, a large NH, low nurse:resident ratio
Perri et al. 2005 (residents with ≥ 9 drugs)	1117	46.5%**	Propoxyphene, promethazine, hydroxyzine, iron supplements and digoxin in greater doses than recommended	No dementia diagnosis, greater number of drugs

**Table 5. continued** PID use in nursing homes according to the Beers criteria

Study	N	Users of PIDs	The most prevalent PIDs	Factors associated with PID use
Niwata et al. 2006 (residents in long-term care hospitals, health facilities for the elderly and NHs)	1669	21.1% independent of diagnoses, 18.0% dependent on diagnoses***	Ticlodipine	Psychotropic drug use, age, medication cost per day, number of drugs
Raivio et al. 2006 (residents in geriatric wards and NHs)	425	36.2***	Temazepam in greater doses than recommended, oxybutynine, dipyrdamole	Number of drugs

\* Beers et al. 1991, \*\* Beers 1997, \*\*\* Fick et al. 2003



**Figure 2.** Drug-drug interactions (adapted from Mallet et al. 2007)

Aging, a high number of drugs, and several prescribers are risk factors for drug-drug interactions (Mallet et al. 2007). In addition, older people are major users of complementary and alternative medicines, some of which are especially marketed to older people; consequently, the elderly are at high risk for herb-drug interactions (Hoblyn & Brooks 2005).

High numbers of medications lead to high risk for adverse drug events. Drug interactions stemming from inhibition of metabolism increase the risk for adverse effects due to excess drug concentrations, whereas drug interactions resulting from induction of metabolism can lead to therapeutic failure due to inadequate drug exposure (Schwartz 2007). Few treatment guidelines based on randomized trials exist

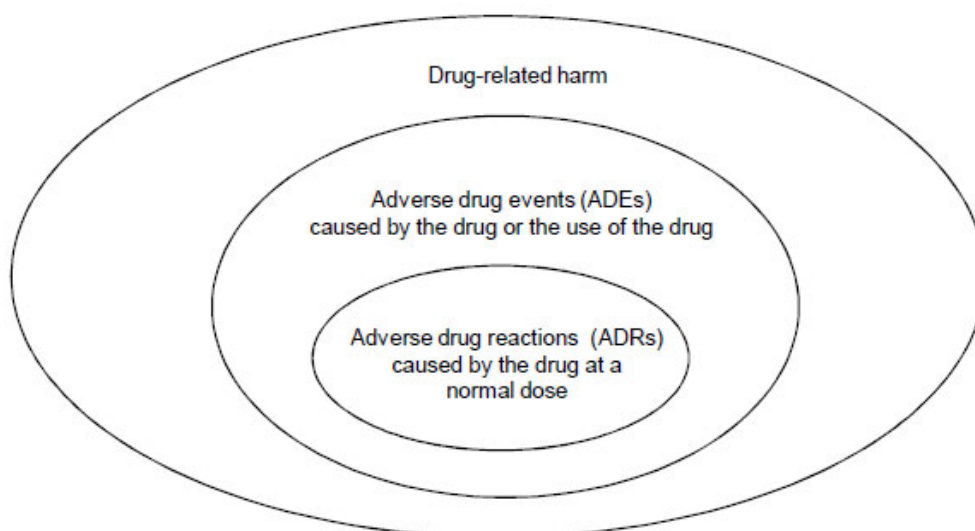
for therapy in patients aged over 80 years, and guidelines developed for younger patients often recommend multiple drug regimens for treating disorders common among the older population: hypertension, diabetes, and coronary artery disease (Schwartz 2007).

In a Norwegian nursing home study, which used the Norwegian Pharmaceutical Products compendium, 9% of 1042 residents were exposed to a potential DDI (Nygaard et al. 2003). The most probable consequences of these DDIs were impaired metabolism and excretion; only three patients used a drug combination that should always be avoided (Nygaard et al. 2003). Because nursing home residents are susceptible to DDIs due to their multiple diseases and polypharmacy, this phenomenon merits further research.

## 2.5 Adverse drug events and reactions

Any substance that is capable of producing a therapeutic effect can also produce unwanted or adverse effects (Edwards & Aronson 2000). An adverse drug event (ADE) is an injury resulting from the use of a drug and includes harm stemming from the drug itself or from use of the drug (Nebeker et al. 2004) (Figure 3). A side effect is a usually predictable or dose-dependent effect of a drug that is not the principal effect for which the drug was chosen; the side effect may be desirable, undesirable or inconsequential (Nebeker et al. 2004). An adverse drug reaction (ADR) is a subtype of side effects that represents an unintentional negative effect resulting from the drug used in normal doses (Nebeker et al. 2004). The World Health Organization has defined an ADR as “a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function” (WHO 1972). Others (Edwards & Aronson 2000) have also suggested the definition “an appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen or withdrawal of the product”. The terms adverse reaction and adverse effect are interchangeable, except that an adverse effect is identified from the point of view of the drug, and an adverse reaction is identified from the point of view of the patient (Edwards & Aronson 2000).

Pharmacovigilance is the study of drug-related injuries intended to provide warning or withdrawal recommendations for pharmaceutical products and is primarily concerned with adverse drug reactions and the properties of the drug in normal use (Nebeker et al. 2004).



**Figure 3.** Drug-related harm (adapted from Edwards & Aronson 2000 and Nebeker et al. 2004)

### 2.5.1 Adverse drug events and reactions in old age

A disproportionately high number of serious adverse drug events occur in older people, even after adjusting for increased drug use (Moore et al. 2007). In a Dutch study of adverse drug reactions among the elderly in general practice, most adverse drug reactions stemmed from antibiotics, antihypertensive drugs, and NSAIDs (Veehof et al. 1999). In a meta-analysis of observational studies, adverse drug events accounted for nearly 5% of all hospitalizations in all age groups, and for 16.6% of hospitalizations among the oldest age group (Beijer & de Blaey 2002). In a US cross-sectional survey of emergency department visits, adverse drug events accounted for 2.5% of all emergency department visits and for 6.7% of hospitalizations (Budnitz et al. 2006). In individuals aged  $\geq 65$  years, ADEs accounted for 5.9% of emergency department visits and 8.8% of hospitalizations (Budnitz et al. 2006). The most common drugs implicated in ADEs were insulin, opioid-containing analgesics, anticoagulants, amoxicillin-containing agents, and antihistamines/cold remedies. These drugs accounted for 27.7% of estimated ADEs. The most common ADEs leading to hospitalization resulted from anticoagulants, insulin, opioid-containing analgesics, oral hypoglycaemic agents and antineoplastic agents; these ADEs accounted for 38.4% of hospitalizations (Budnitz et al. 2006). A US cohort study that included

almost 29 000 nursing home resident-months identified 546 ADEs (1.89 per 100 resident-months), of which 51% were considered preventable (Gurwitz et al. 2000).

Factors responsible for increased ADEs in older people seem to be multiple drug use, including prescription and over-the-counter drugs, increased drug-drug interactions, pharmacokinetic and pharmacodynamic changes, drug therapy compliance, and aging itself (Beyth & Shorr 1999). Some of the hazards attributed to multiple drug use may actually be related to the comorbidities for which the drugs are prescribed (Hilmer et al. 2007b).

In frail older people, ADEs may be numerous. ADEs may present as falls and confusion (Hilmer et al. 2007b). Among those elderly with multiple comorbidities and minimal functional reserve, and for whom evidence of the effectiveness of medication use to guide prescribing is limited, the impact that a change in medication regime has on physical function may be a clinically useful marker for drug response (Hilmer & Gnjdjic 2009). The Kuopio 75+ study reported a significant difference between self-reported ADRs (11.4%) and physician-observed ADRs (24%) (Lampela et al. 2007). The authors suggest that older people may ignore ADRs and consider them an unavoidable part of aging. Consequently, a physician should remain attentive to potential ADRs even though the elderly patient may not complain of drug-related problems (Lampela et al. 2007). The general wisdom in geriatric prescribing of initiating new drug regimens with low doses and slowly increasing the dosage is based on a concern for adverse drug reactions (McLean & Le Couteur 2004).

### **2.5.2 Adverse drug reactions of psychotropic drugs**

Psychotropic drugs, along with anticoagulants, are the most common medications associated with preventable ADRs (Gurwitz et al. 2000). Older people may suffer from falls, as well as from anticholinergic and cognitive adverse drug reactions of these drugs (Leipzig et al. 1999, Cumming 1998). A systematic review consisting of 29 studies identified psychotropics, including benzodiazepines, antidepressants, and antipsychotics, as the main group of drugs associated with falls in older people (Hartikainen et al. 2007). The Health, Aging and Body Composition Study of home-dwelling older people associated the combined use of central nervous system drugs (benzodiazepines, opioid-receptor agonists, antipsychotics, and antidepressants) with recurrent falls and cognitive decline (Hanlon et al. 2009, Wright et al. 2009). A recent review of psychotropic drugs and falls consisting of 17 studies found strong evidence that the use of multiple drugs, antidepressants, and anti-anxiety drugs is associated with higher risk for falls (Sterke et al. 2008). The evidence for the association of other

psychoactive drugs with risk for falls was limited or inconclusive. The Kuopio 75+ study compared the risk of mortality in home-dwelling elderly with a diagnosis of dementia. Compared to non-users of psychotropics, the hazard ratio for mortality among individuals with antipsychotics as their only psychotropic medication was 2.75, and among concomitant users of all kinds of psychotropics, 1.76 (Hartikainen et al. 2005).

Selective serotonin reuptake inhibitors (SSRIs) can cause hyponatremia and serotonergic syndrome, as well as bleeding when combined with non-steroidal anti-inflammatory drugs (NSAIDs). Tricyclic antidepressants can lengthen QT time and cause cardiac dysrhythmias (van Noord et al. 2009, Pelkonen & Ruskoaho 2003).

Atypical antipsychotic drugs have been associated with several ADRs, including cerebrovascular events (Wooltorton 2002b, Wooltorton 2004), cardiac events (Wooltorton 2002a), hyperglycemia, and diabetes (Wooltorton 2004), and higher mortality (Singh & Wooltorton 2005). In a Canadian nursing home study, facilities with more intense antipsychotic drug use presented higher mortality rates despite more favourable clinical characteristics at resident admission (Bronskill et al. 2009). The risk of death is highest after 30 days of initiation of an atypical antipsychotic (OR 3.2, 95% CI, 2.8 to 3.7) (Rochon et al. 2008). The risk of death is even higher among users of conventional antipsychotics (Wang et al. 2005). In a Finnish survey of 49 medico legal autopsies, sudden unexpected death was especially associated with thioridazine (Mehtonen et al. 1991). A meta-analysis of 15 trials of atypical antipsychotics reported the following ADRs: somnolence, urinary tract infection, extrapyramidal effects, abnormal gait, edema, cerebrovascular adverse events (Schneider et al. 2006), and elevated risk of mortality (Schneider et al. 2005). In a Finnish follow-up study, however, conventional and atypical antipsychotics failed to raise the risk of mortality or hospital admissions among nursing home and geriatric ward patients with dementia, and in multivariate analysis, atypical antipsychotics seemed to decrease the risk of mortality (Raivio et al. 2007).

Whether an unwanted symptom is an ADR or results from the underlying disease or condition for which the drug was prescribed is not self-evident. For example, a US study consisting of over 34 000 nursing home residents found an association between falls and insomnia; surprisingly, hypnotic use failed to predict falls (Avidan et al. 2005). Another US study compared hip fracture rates in the states of New York and New Jersey after the state of New York implemented a regulatory action on prescribing benzodiazepine. The regulatory action resulted in a 60% reduction in benzodiazepine use in New York. Even so, the incidence of hip fractures remained unchanged (Wagner et al. 2007).

Appropriate psychotropic prescribing may reduce the incidence of ADRs. Atypical antipsychotics, for example, enjoy advantages over conventional antipsychotics, including fewer extrapyramidal ADRs (Jeste et al. 1999), and short-acting benzodiazepines are preferable to long-acting benzodiazepines (Fick et al. 2003). Because tricyclic antidepressants can cause anticholinergic ADRs, and long half-life fluoxetine can induce excessive CNS stimulation, avoiding such drugs has been recommended (Fick et al. 2003, Leipzig et al. 1999).

### **2.5.3 Adverse drug reactions of potentially inappropriate drugs**

In a French study that comprised over 2000 older patients admitted to an acute geriatric unit and used modified Beers 1997 criteria of potentially inappropriate drugs found that 66% of patients received PIDs on hospital admission (Laroche et al. 2007b). The most common PIDs were anticholinergic antidepressants, cerebral vasodilators, and long-acting benzodiazepines. The prevalence of ADRs was 20% among patients receiving PIDs, and 16% among patients receiving no PIDs. After adjusting to confounding factors, however, no PIDs were associated with increased risk for ADRs. The main preventable factor in ADRs seems to be reducing the number of drugs (Laroche et al. 2007b).

An Italian study of 500 recently hospitalized elderly patients investigated the relationship between PIDs independent of diagnoses according to the Beers 2003 criteria and the Loss of Activities of Daily Living (Corsonello et al. 2009). At hospital admission, 21% of patients were taking at least one PID, and 10% of patients received new prescriptions of at least one PID during their hospital stay. The most prevalent PIDs at baseline were ticlodipine, doxazosin, and amiodarone. The most frequently prescribed new PIDs were ticlodipine, long-acting benzodiazepines, and ferrous sulphate > 325 mg/day. Functional decline was unassociated with PID use, but was strongly associated with ADRs to any drugs (Corsonello et al. 2009).

A US survey investigated inappropriate medication as a risk factor for one-year self-reported ADRs (Chrischilles et al. 2009). The study cohort comprised over 600 elderly people with a mobility disability, and the criteria for inappropriate medication use were PIDs independent of and dependent on diseases and conditions according to the Beers 1997 criteria, DDIs and therapeutic duplication. Of all the participants, 51% were exposed to inappropriate medication use, 32% used PIDs independent of diseases or conditions, 30% were experienced a drug-disease interaction, and 6% were exposed to therapeutic duplication. The most frequent PIDs included propoxyphene, amitriptyline, and oxybutynine. The one-year self-reported prevalence



of ADR was 30% among participants using PIDs, and 14% among those using only appropriate medications. In multivariate analysis, all measures of inappropriate medication use were significantly associated with self-reported ADRs (Chrischilles et al. 2009).

In a US study with a sample of nearly 17 000 community-dwelling elderly, the use of PIDs according to the Beers 2003 criteria raised the risk for health care utilization 1.5-2 times higher than did the non-use of PIDs (Fick et al. 2008).

In another US survey investigating older adults' visits to the emergency department due to ADEs, nearly 4% of emergency department visits involved PIDs (according to the Beers 2003 criteria) (Budnitz et al. 2007). Warfarin, insulin, and digoxin accounted for 33% of the ADEs leading to emergency department visits. Accounting for the frequency of outpatient prescription, the risk for emergency department visits due to warfarin, insulin, and digoxin was 35 times greater than for PIDs (Budnitz et al. 2007). Adverse healthcare outcomes of PIDs appear in Table 6.

**Table 6.** Adverse healthcare outcomes of PIDs in nursing homes according to the Beers criteria (modified from Jano & Aparasu 2007)

Authors	N	Design	Mortality	Hospitalization	Other outcome
Gupta et al. 1996	19932	retrospective cross-sectional	non-significant		↑ Costs
Lau et al. 2005	3 372	retrospective cohort	↑ OR 1.28 (95% CI, 1.05-1.55)	↑ OR 1.27 (95% CI, 1.09-1.47)	
Klarin et al. 2005 (incl. sheltered housing)	128	retrospective cohort	non-significant	non-significant	
Perri et al. 2005	1117	retrospective cohort			↑ OR 2.34 (95% CI, 1.61 to 3.40) [death, hospitalization or emergency department visit]
Raivio et al. 2006	195	retrospective cohort	non-significant	non-significant	

## 2.6 Tools for improving the quality of prescribing

Tools for assessing the appropriateness of older people's drug therapies have been developed to prevent drug therapy-related adverse events in older patients (Fick et al. 2003, Beers et al. 1991, Beers 1997, McLeod et al. 1997, Naugler et al. 2000). Measures for assessing prescribing may be criterion-based and explicit or judgement-based and implicit (Spinewine et al. 2007). Criteria used with prescription data alone or combined with clinical data may include lists of "drugs to avoid" or drugs that may interact with each other. Criteria for detecting underprescribing may indicate an evidence-based need for using a certain drug for a specific condition if no contraindication exists (Barry et al. 2007). Misprescribing criteria focus on drug choice, dose, drug interactions, duration of drug therapy, duplication, and follow-up (Spinewine et al. 2007).

The explicit criteria are drug- or disease-oriented, relatively easy to use, and may define the minimum level of quality of prescribing (Spinewine et al. 2007). Explicit criteria include the Beers criteria for older adults (Fick et al. 2003, Beers et al. 1991, Beers 1997) as well as the McLeod (McLeod et al. 1997) and Zhan (Zhan et al. 2001) criteria, the Improving Prescribing in the Elderly Tool (IPET) (Naugler et al. 2000), Assessing Care of the Vulnerable Elder (ACOVE) (Shekelle et al. 2001a and 2001b), Screening Tools to Alert Doctors to the Right Treatment (START) (Barry et al. 2007), the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) (Gallagher & O'Mahony 2008), and the French consensus panel list of potentially inappropriate medications in the elderly (Laroche et al. 2007a). At the moment, Finnish experts in geriatric drug therapy are preparing a database to support appropriate prescribing to older adults in Finland (Mäntyranta T., oral communication 10.3.2010).

Some of the above-mentioned tools were developed using the Delphi consensus method (Fick et al. 2003, Beers et al. 1991, Beers 1997, Barry et al. 2007, Gallagher & O'Mahony 2008, Laroche et al. 2007a). With this method, a panel of experts is presented with statements. The experts then individually rate their level of agreement with the statements and may supplement them or suggest other statements. This procedure is repeated until the experts reach consensus. Even though the experts in the Delphi process may use evidence-based medicine in formulating the statements, the tool must nevertheless be validated.

Explicit drug-drug interaction criteria are often embedded in computerized programs such as Medi-span ([www.medispan.com](http://www.medispan.com)), Lexi-Comp ([www.lexi.com](http://www.lexi.com)), CPOE-CDS (Rochon et al. 2006), or Swedish, Finnish, Interaction X-referencing, SFINX (Lääkeinteraktiot SFINX). Introduced in 2006, SFINX is a commercial medical

drug-drug interaction database that is updated quarterly by specialists in clinical pharmacology at the Turku University Hospital, the Karolinska Institutet, and the Stockholm county council (Läakeinteraktiot SFINX). A Swedish interaction database ([www.fass.se](http://www.fass.se)), which preceded SFINX, is now embedded in it. In October 2009, the SFINX database contained more than 9000 DDIs. The clinical significance of the interactions is classified from A to D. Significance level A means the interaction is clinically insignificant, and significance level D means the interaction is clinically significant and that the combination should be avoided.

A medication exposure measure associated with functional outcomes may also be a useful prescribing tool (Hilmer & Gnjidic 2009). The Drug burden index is an integrated model of exposure to medications most consistently associated with functional impairment (e.g. medications with anticholinergic and sedative effects) (Hilmer et al. 2007a). The Drug burden index is a linear additive model that incorporates pharmacokinetics (dose) and pharmacodynamics (dose response, maximal effect) to measure cumulative exposure to anticholinergic and sedative medications. The Drug burden index has been independently associated with the impairment of physical performance and cognition (Hilmer et al. 2007a).

Implicit criteria include clinical assessment of the appropriateness of drug therapy and focus on the patient rather than on drugs or diseases (Spinewine et al. 2007, Roth et al. 2009). Compared to explicit criteria, implicit criteria are more comprehensive, but also more complicated to use (Spinewine et al. 2007).

The Medication Appropriateness Index (MAI) classifies patient's every medication as appropriate, marginally appropriate, or inappropriate based on ten criteria: indication, effectiveness, dosage, directions, practicality, drug-drug interactions, drug-disease interactions, unnecessary duplication, duration, and cost (Spinewine et al. 2006, Samsa et al. 1994). This index produces a summated score to provide an overall measure of the appropriateness of medication use. However, the index fails to take into account underprescribing, drug allergy, adverse drug reactions, and compliance, and is tedious to use (Spinewine et al. 2006, Samsa et al. 1994). According to the authors, the index has excellent reliability and validity as well as good interrater and intrarater agreement (Samsa et al. 1994). However, the index has shown lower reliability in assessments by other researchers, and some have offered recommendations for improving the instrument's reliability and validity (Spinewine et al. 2006). Nevertheless, the MAI is a comprehensive, if time-consuming (Stuijt et al. 2008), measure for assessing the appropriateness of an individual patient's drug therapy.

Tools for improving the quality of prescribing have some inconveniences. Explicit criteria have low specificity, and consequently, a drug labeled inappropriate for older adults may in some cases be appropriate or otherwise harmless. In addition, these criteria fail to take into account an individual patient's characteristics, comorbidities, or adherence. Moreover, the real problem in prescribing for the elderly may actually be underprescribing (Spinewine et al. 2007). Implicit criteria are complicated and time consuming, and their reliability may depend on the expertise of the applier (Spinewine et al. 2007, Roth et al. 2009).

### 3 The aims of the study

This study explores dimensions of appropriate prescribing among elderly nursing home residents in Helsinki. The specific aims were:

1. To describe the use of psychotropic drugs and associated factors among residents with and without dementia (I);
2. To assess the prevalence of laxatives and to identify factors and medications associated with the regular use of laxatives (II);
3. To clarify the use of vitamin D and calcium and the associations between vitamin D and calcium supplementation and nutritional status, diseases, and daily routines of nutritional care (III);
4. To describe the prevalence of potentially inappropriate drugs according to the Beers 2003 criteria, and potential class D drug-drug interactions according to the SFINX database ("clinically significant interaction, and the combination should be avoided") (IV);
5. To describe differences in drug prescribing in public and private nursing homes.

## 4 Subjects and methods

### 4.1 Study populations

The cross-sectional material for this study was collected during February 2003 from all nursing homes in Helsinki, Finland as part of a larger project investigating the nutritional status of nursing home residents (Muurinen et al. 2003). The inclusion criteria for Studies I, II, and IV were long-term residency, the availability of sufficient information about demographic factors and medication, willingness to participate, and age  $\geq 65$  years. The inclusion criteria for Study III were long-term residency, sufficient information on the use of vitamin D and calcium supplements, and willingness to participate.

In February 2003, 1088 persons were residing in 4 public nursing homes, and 1336 in 16 private nursing homes. Of the 2424 total residents, 132 (5.4%) were in respite care for one to two weeks, 150 (6.2%) were in short-term rehabilitation, and 22 (0.9%) refused to participate. Of the residents assessed, 2025 possessed sufficient medical and demographic data for Studies I, II, and IV. Residents aged  $< 65$  years ( $n=38$ ) were excluded, leaving 1987 residents (82%) who were eligible for further analysis. For Study III, 2114 long-term residents were willing to participate and had sufficient information on the use of vitamin D and calcium supplements (Figure 4).

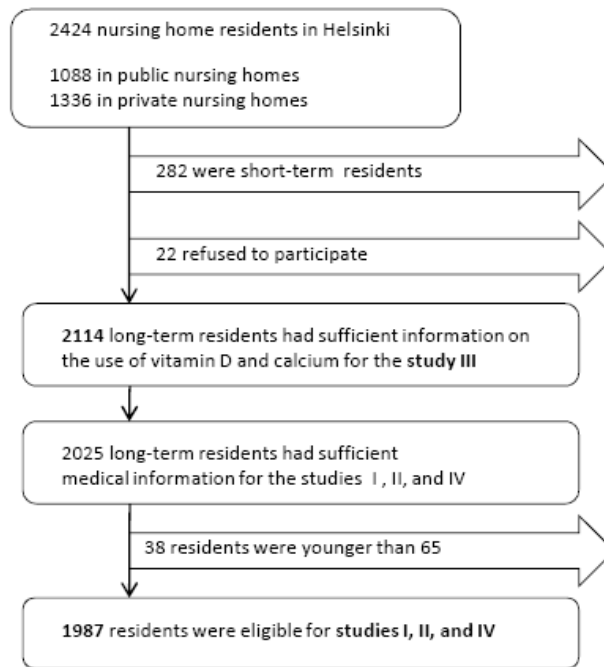
### 4.2 Methods

#### 4.2.1 Background data

The study questionnaire (Appendix 1) consisted of the Mini Nutritional Assessment and a questionnaire about the resident's background information and health status, including his or her medication records.

Nurses trained to use the MNA and to complete the study questionnaire were assigned to each home ward. These nurses organized the data collection, assessed the residents' health status and retrieved data on demographic factors, regularly administered medications, and diagnoses from the residents' medical records.

Residents whose medical records indicated a diagnosis of dementia or who were using either anticholinesterase or memantine were classified as having a diagnosis of dementia. The criterion for depression was a Resident Assessment Instrument (RAI)



**Figure 4.** Flow chart of the study populations

depression score of  $\geq 3$  (range 0 to 14) (Burrows et al. 2000). The Charlson comorbidity index served to assess multimorbidity (Charlson et al. 1987). Residents' mobility was dichotomized into unable to move independently (bed-ridden residents and residents using a wheelchair) and others.

Each resident was assessed using the Mini Nutritional Assessment (MNA). The overall MNA score distinguishes elderly patients: i) with good nutritional status (MNA score 24-30 points), ii) at risk for malnutrition (MNA score 17-23.5), and iii) who are malnourished (MNA score  $< 17$ ) (Vellas et al. 1999).

Whether a resident received snacks between meals was inquired with a yes/no question. Snacks in Finland usually mean yogurt, dark bread, or fruits. How much of the main meal the resident eats on average was inquired with answer options "less than half, half, nearly all or all". This response was dichotomized to "eating less than half or half" and to "nearly all or all". The nurses were instructed to make their estimations of the amount of food eaten as well as of other factors related to nutritional care over the preceding three months.

All data were collected and analyzed anonymously. Patients and proxies were informed about the study and their consent was an inclusion criterion. The City of Helsinki ethics committee granted permission for the study.

### 4.2.2 Medication use

The medication data were collected as point prevalence in February 2003. Nursing home personnel either handwrote the medication record onto the resident's study questionnaire or printed the medication record as an appendix.

A resident was classified as a drug user if his or her medication record indicated a regular sequence of drug administration. Others, including those whose medication records indicated permission for the nurse to administer the drug, if necessary, on an as-needed basis, were classified as non-users. The drugs were coded according to their Anatomical Therapeutic Chemical (ATC) classification index (ATC DDD 2009). Nine or more drugs daily was the cut-point for polypharmacy (Hanlon et al. 2001).

### 4.2.3 Psychotropic medication

This study investigated the use of the following psychotropic drugs: antipsychotics N05A, antidepressants N06A, anxiolytics N05B, hypnotics N05C, and antidementia drugs N06D (ATC DDD 2009).

Antipsychotics were divided into conventional (chlorpromazine, chlorprothixene, flupentixol, fluphenazine, haloperidol, levomepromazine, melperone, pericyazine, perphenazine, promazine, sulpiride, thioridazine, zuclopenthixol) and atypical antipsychotics (clozapine, olanzapine, quetiapine, risperidone).

Antidepressants were classified as selective serotonin re-uptake inhibitors (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline), tricyclic antidepressants (amitriptyline, clomipramine, doxepin, nortriptyline, trimipramine), and other antidepressants.

Long-acting benzodiazepines (diazepam, chlordiazepoxide) (Fick et al. 2003) were separated from other benzodiazepine anxiolytics (alprazolam, lorazepam, oxazepam) and from anxiolytics other than benzodiazepines (buspirone, clomethiazole).

All hypnotics (midazolam, nitrazepam, temazepam, zopiclone, zolpidem) were coded into a single group.

The antidementia drugs used were divided into anticholinesterases (donepezil, galantamine, rivastigmine) and memantine.

Mean and median doses for the most frequently used preparations of conventional and atypical antipsychotics, antidepressants, anxiolytics, and hypnotics were compared with the Defined Daily Dose (DDD), the assumed average daily maintenance dose for a drug used for its main indication in an adult (ATC DDD 2009).



#### 4.2.4 Laxatives

The following laxatives were available in Finland at the time of data collection: senna, bisacodyl, and sodium picosulfate (stimulant laxatives A06AB); seeds of *plantago ovata* (bulk laxatives A06AC); and saline laxatives, macrogol, lactulose, and lactitol (osmotic agents A06AD). In addition, the following medications were classified as laxatives, per the suggestions of prior studies (DiPalma 2004), although they are used mainly for other indications: metoclopramide, cisapride, and cholinergic agents carbamylcholine, pyridostigmine, and distigmine (neuromuscular agents).

Drugs which, according to the medical literature (van Dijk et al. 1998, Harari et al. 1995, Monane et al. 1993, Dosh 2002), may cause constipation were classified as potentially constipation-inducing drugs. In addition, drugs which, according to the product summaries in *Pharmaca Fennica* 2006, may induce constipation were taken into analyses; we also included into our analyses other drugs of that same class.

The drugs classified as potentially constipation-inducing are as follows: acetazolamide, antiepileptics, baclofen,  $\alpha$ 1-adrenoceptor antagonists, histamine H2-receptor antagonists, proton pump inhibitors, antacids, bisphosphonates,  $\beta$ -adrenoceptor antagonists, diuretics, HMG-CoA reductase inhibitors (statins), lipid-lowering drugs other than statins, ACE inhibitors, verapamil and nifedipine, calcium channel antagonists other than verapamil and nifedipine, opioids, paracetamol, acetylsalicylic acid, cyclo-oxygenase-2 selective NSAIDs, nonselective NSAIDs, antiparkinsonian drugs, anticholinergic drugs for urinary incontinence, calcium supplements, iron supplements, atypical antipsychotics, conventional antipsychotics, all antidepressants, tricyclic antidepressants, SSRIs, antidepressants other than tricyclics, and SSRIs and anxiolytics.

#### 4.2.5 Vitamin D and calcium supplements

The use of vitamin D and calcium supplementations were inquired with yes/no-questions such as "Does the resident receive a vitamin D supplement?" or "Does the resident receive a calcium supplement?" Those answering "yes" or whose medical record indicated that they receive calcium or vitamin D supplements were considered supplement users. Because the use of vitamin D and calcium supplements was also inquired with a specific question in the questionnaire about the resident's background information and health status, an incomplete medication record was not an exclusion criterion for Study III, and consequently, the study population (N=2114) was larger than in Studies I, II, and IV (N=1987).

#### **4.2.6 Potentially inappropriate medications**

The Beers criteria 2003 identify PID use among older adults both independent of diagnoses or conditions as well as taking them into account (Fick et al. 2003). This study used the criteria independent of diagnoses or conditions. The following drugs included in the criteria were unavailable in Finland in 2003: pentazocine, trimethobenzamide, methocarbamol, metaxalone, cyclobenzaprine, flurazepam, quazepam, halazepam, chlorazepate, methyldopa, reserpine, chlorpropamide, dicyclomine, propantheline, chlorpheniramine, cyproheptadine, promethazine, dexchlorpheniramine, meperidine, ticlodipine, oxaprozin, cascara sagrada, Neoloid (castor oil), guanethidine, guanadrel, doxazosin, mesoridazine, mineral oil, cimetidine, ethacrynic acid, desiccated thyroid, and amphetamines.

#### **4.2.7 Drug-drug interactions**

Swedish, Finnish, Interaction X-referencing SFINX is a commercial medical drug-drug interaction (DDI) database. Introduced in 2006, SFINX is updated quarterly by specialists in clinical pharmacology at the Turku University Hospital, Finland as well as at the Karolinska Institutet and Stockholm county council, Sweden (Lääkeinteraktiot SFINX). The interactions in the SFINX database are classified according to their clinical significance and level of documentation. Clinical significance is classified from A to D; A means the interaction is clinically insignificant, whereas D means the interaction is clinically significant and the combination should be avoided. This study investigates the prevalence of potential class D DDIs in the nursing home population.

#### **4.2.8 Statistical methodology**

The research secretary entered the data into Microsoft Excel 2002. Residents' medication lists were checked, and input errors were corrected one by one. The coded data were analyzed using the Statistical Package for the Social Sciences (SPSS) versions 12.0.1 and 15.0, and NCSS statistical analysis and graphics software.

Drug users were compared to non-users with the  $\chi^2$ -test or with Fischer's exact test, when appropriate. The independent sample T-test served to compare mean ages and numbers of daily drugs. P-values of  $< 0.05$  were considered statistically significant. Confidence intervals were calculated with Confidence Interval Analysis version 1.0 (Gardner & Altman 1989).

Multivariate analyses were performed with NCSS using logistic regression analysis. In the study on the use of laxatives, multivariate logistic regression analysis served to determine which statistically significant variables in the univariate analyses were independently associated with the use of laxatives. Age > 80 years, previous stroke, Parkinson's disease, inability to move independently, poor Mini Nutritional Assessment score (< 17), a fluid intake of less than five glasses daily, chewing problems, a high number of drugs other than laxatives and constipation-inducing drugs, and snacks between meals served as covariates in multivariate analysis. In the vitamin D and calcium study, age > 80 years, gender, poor Mini Nutritional Assessment score (< 17), a poor Activities of Daily Living score (ADL) ( $\geq 4$ ), lactose intolerance, constipation according to the MNA questionnaire, previous hip fracture, eating half or less of meal proportions offered, snacks between meals, and weight monitoring no more than once annually served as covariates.

## 5 Results

### 5.1 Baseline data

Of the 1987 elderly residents assessed in Studies I, II, and IV, 80.7% were female. The residents' mean age was 83.7 (SD 7.7). The percentage of widowed residents was 53%, and 53.5% had received no more than a primary school education. The proportion of residents with a diagnosis of dementia was 69.5%. The mean number of drugs consumed daily was 7.9 (SD 3.6). The mean number of drugs in residents with a diagnosis of dementia was 7.4 (SD 3.3), and in residents with no diagnosis of dementia, 9.06 (SD 3.9). Females consumed a higher number of daily drugs than did men: 8.03 (SD 3.6) and 7.4 (SD 3.5), respectively. In Study III (n=2114), the mean age was 83 years, and 80.7% were female.

Residents in private nursing homes (N=914) were older, more often female, widowed, with a diagnosis of dementia, better nourished, and with a higher Charlson comorbidity index than were residents in public nursing homes (N=1073). Residents in public nursing homes more often had stroke and poor mobility than did residents in private nursing homes (Table 7).

### 5.2 Psychotropic medication

Altogether 79.7% of all residents were prescribed psychotropic drugs (Table 8). Antipsychotic drugs were administered to 42.6% of residents, and 5.3% of all residents received  $\geq 2$  antipsychotic drugs. Altogether 18.9% of the residents received conventional antipsychotics, and 27.0% received atypical antipsychotics. The prevalence of antipsychotics was higher among younger residents: 51.8%, 42.1%, and 31.3% among residents aged 65 to 79 years, 80 to 90 years, and  $> 90$  years, respectively.

Of all residents, 44.6% received antidepressants, and the percentage of residents receiving more than one antidepressant was 2.7%. SSRIs were the most common antidepressants, used by 27.6% of residents. Fluoxetine, an antidepressant considered inappropriate for the elderly because of overstimulation of the central nervous system, sleep disturbances, and agitation (Fick et al. 2003), was administered to 1.3% of residents, and 3.1% received tricyclic antidepressants. Of all residents, 17.6% received antidepressants other than SSRIs or tricyclics; 11.4%

**Table 7.** Baseline characteristics of the nursing home residents

	All residents (n=1987)	Females (n=1604)	Males (n=383)	p-value	Residents in public nursing homes (n=914)	Residents in private nursing homes (n=1073)	p-value
Age, years, mean (SD)	83.7 (7.7)	84.6 (7.4)	80.1 (7.8)	<b>&lt;0.001*</b>	83.02 (8.0)	84.34 (7.4)	<b>&lt;0.001**</b>
Females, %	80.7	100	0	*	77.6	83.3	<b>0.001*</b>
Widowed, %	53	58.3	30.8	<b>&lt;0.001*</b>	49.7	56.7	<b>0.002*</b>
Education primary school or less, %	53.5	54.0	51.7	0.14*	64.2	60.0	0.071*
Dementia, %	69.5	71.4	60.8	<b>&lt;0.001*</b>	66.7	71.7	<b>0.017*</b>
RAI depression score $\geq 3$ , %	37.9	40.8	25.7	<b>&lt;0.001*</b>	37.5	38.6	0.69*
Stroke, %	29.7	26.2	31.6	<b>0.03*</b>	32.0	27.7	<b>0.05*</b>
Unable to move independently, %	30.4	31.0	27.2	0.12*	36.0	25.6	<b>&lt;0.001*</b>
Charlson comorbidity index	2.12 (1.2)	2.13 (1.2)	2.08 (1.3)	0.41**	2.06 (1.2)	2.18 (1.2)	<b>0.027**</b>
Diabetes mellitus	16.9	17.0	16.7	0.89*	17.9	16.0	0.26*
Parkinson's disease	5.0	5.2	4.2	0.39*	5.5	4.7	0.41*
Swallowing problems	24.6	25.7	20.2	<b>0.02*</b>	22.7	26.3	0.07*
MNA score < 17	28.4	29.8	22.9	0.008*	31.6	25.7	<b>0.004*</b>
MNA score > 23.5	11.2	10.0	16.4	<b>&lt;0.001*</b>	9.5	12.7	<b>0.026*</b>
Mean number of drugs (SD)	7.9 (3.6)	8.03 (3.6)	7.38 (3.5)	<b>0.001**</b>	8.28 (3.7)	7.58 (3.4)	<b>&lt;0.001**</b>
Taking $\geq 9$ drugs daily, %	40.3	41.0	37.2	0.17*	44.6	36.6	<b>&lt;0.001*</b>

**Table 8.** The use of psychotropic drugs in nursing homes in Helsinki

	Residents n=1987, %	With dementia n=1380, %	Without dementia n=607, %	p-value*	Females n=1604, %	Males n=383, %	p-value*
Psychotropic drug	79.7	77.6	84.5	<b>&lt;0.001</b>	80.0	78.6	0.56
Antipsychotic drug	42.6	43.3	41.0	0.34	41.5	47.1	<b>0.05</b>
Conventional	18.9	17.8	21.3	0.07	17.8	23.2	<b>0.02</b>
Atypical	27.0	28.3	24.2	0.06	26.8	27.9	0.68
Antidepressant	44.6	41.4	51.9	<b>&lt;0.001</b>	46.4	37.2	<b>0.001</b>
SSRIs	26.7	24.8	31.0	<b>0.004</b>	27.7	22.4	<b>0.04</b>
Tricyclics	3.1	2.4	4.6	<b>0.008</b>	3.2	2.3	0.36
Other	17.6	15.6	22.1	<b>&lt;0.001</b>	18.3	14.8	0.11
Anxiolytic drug	26.3	25.3	28.5	0.13	26.1	27.3	0.61
Long-acting BZD	2.4	1.5	4.4	<b>&lt;0.001</b>	2.3	3.1	0.34
Other BZD	22.6	22.2	23.6	0.52	22.8	22.1	0.79
Other than BZD	2.5	2.6	2.1	0.54	1.9	4.9	<b>&lt;0.001</b>
Hypnotics	27.5	22.8	38.1	<b>&lt;0.001</b>	26.8	30.5	0.14
Anticholinesterases	7.2	10.4	NA	NA	7.4	6.5	0.56
Memantine	0.2	0.3	NA	NA	0.2	0.0	0.33

\* X<sup>2</sup>-test, residents with dementia compared with residents without dementia or females compared with males.

Statistically significant p-values ( $\leq 0.05$ ) marked with bold letters. BZD=benzodiazepine. NA=not applicable.

received mirtazapine. Of those residents diagnosed with depression (RAI depression score  $\geq 3$ ), 47.3% used antidepressants.

One or more anxiolytic drugs were regularly administered to 26.3% of residents, and 27.5% used hypnotics.

Of those residents diagnosed with dementia, 10.4% used cholinesterase inhibitors and 0.2% used memantine. Two residents received both memantine and cholinesterase inhibitor (Table 8).

Men used any antipsychotics and conventional antipsychotics significantly more often than did women; the use of anxiolytics other than benzodiazepines was also more common among men. Women used SSRIs more often than did men (Table 8).

The dosages of various psychotropic drugs were moderate. Haloperidol, used by 4.7% of residents, had a mean dose of 1.5 mg (18.8% of DDD), and the median dose was 1 mg (range 0.5-9 mg). Risperidone, used by 16.6% of residents, had a mean dose of 0.9 mg (15% of DDD), and the median dose was 0.75 mg (range 0.25-7 mg). The mean dose of citalopram, used by 24.1% of residents, was 20.2 mg (101% of

DDD), and the median dose was 20 mg (range 10-40 mg). Oxazepam was received by 14.0% of residents; its mean dose was 17.3 mg (34.6% of DDD), and its median dose was 15 mg (range 3.75-60 mg). Of all residents, 17.7% received temazepam; the mean dose was 19.1 mg (95.5% of DDD), and the median dose was 20 mg (range 10-40 mg).

## 5.3 Laxatives

Of all residents, 55.3% (n=1099) received laxatives regularly. Most of the laxative users received osmotic agents (45.8%). The use of stimulant laxatives (14.3% of all residents) was also common. Bulk laxatives were used by 4.0% of residents, and neuromuscular agents by 1.4%. In addition, 0.9% of residents were using unidentified laxatives. Of all residents, 11.5% used  $\geq 2$  different laxatives simultaneously (see Paper II: Results).

The factors associated with regular laxative use in univariate analyses were advanced age, previous stroke, Parkinson's disease, inability to move independently, malnutrition (MNA score < 17), a fluid intake of less than five glasses daily, and chewing problems. Residents eating snacks between meals used laxatives less often than did those eating no snacks: 42.3% and 51.0%, respectively.

The potentially constipation-inducing drugs associated with regular laxative use were opioids, antacids, diuretics, tricyclic antidepressants, cholesterol-lowering drugs other than statins, histamine-2 blockers, non-selective NSAIDs, anticholinergic drugs for urine incontinence, and calcium channel blockers other than verapamil and nifedipine. Of all residents, 58.2% used one or more of these constipation-inducing drugs found in the univariate analysis; 63.0% of laxative users and 52.3% of laxative non-users received one or more constipation-inducing drugs (p-value < 0.001). The mean number of daily drugs, excluding laxatives and drugs associated with laxative use, was 6.6 (SD 3.1) for laxative users and 6.2 (SD 3.1) for non-users (p=0.001).

We performed a multivariate logistic regression analysis in which age over 80 years, gender, previous stroke, Parkinson's disease, inability to move independently, a poor MNA score (< 17), a fluid intake of less than five glasses daily, chewing problems, eating snacks between meals, and a high number (> 7) of drugs other than laxatives or constipation-inducing drugs found in the univariate analysis served as covariates. In this analysis, age over 80 years (OR 1.29 [95% CI, 1.03 to 1.60]), the inability to move independently (OR 1.80 [95% CI, 1.42 to 2.28]), a poor MNA score (< 17) (OR 1.51 [95% CI, 1.19 to 1.93]), chewing problems (OR 1.27 [CI, 95% 1.00

to 1.61]), Parkinson's disease (OR 1.63 [95% CI, 1.01 to 2.64]), and a high number (> 7) of drugs other than laxatives and constipation-inducing drugs found in the univariate analysis (OR 1.06 [95% CI, 1.03 to 1.09]) were associated with the use of laxatives. Eating snacks between meals (OR 0.74 [95% CI, 0.60 to 0.90]) was associated with lower risk for laxative use.

## 5.4 Vitamin D and calcium supplements

Nearly one third (32.9%) of all nursing home residents (n=2114) received vitamin D supplementation, and 29.2% were administered calcium supplements. Altogether 20.0% of residents received both vitamin D and calcium supplementation.

Factors associated with more frequent vitamin D supplementation were female gender ( $p=0.01$ ), lactose intolerance ( $p < 0.001$ ), better nutritional status ( $p=0.005$ ), a higher Activities of Daily Living (ADL) score ( $p=0.004$ ), eating snacks between meals ( $p < 0.001$ ), and regular weight monitoring ( $p < 0.001$ ). Residents with constipation, according to the MNA questionnaire, received vitamin D supplementation less often than did those without constipation ( $p=0.008$ ).

Residents receiving calcium supplementation had constipation less often than did residents receiving no calcium supplements: 40.6% vs. 46.6%,  $p=0.01$ ). Of those residents with lactose intolerance, 44.4% received calcium supplementation compared to 27.6% who were lactose tolerant  $p<0.001$ ).

The dosage of vitamin D varied between 3 µg and 40 µg (120-1600 IU). Of all residents, 21.2% received vitamin D in doses of  $\geq 10$  µg (400 IU), the recommendation at the time of the data collection (Ministry of Social Affairs and Health 2003). Only 3.5% of residents received vitamin D in excess of 20 µg (800 IU), an effective dose for preventing fractures.

In logistic regression analysis where age, gender, malnutrition (MNA score < 17), poor physical functioning (Activities of Daily Living score  $\geq 4$ ), lactose intolerance, constipation, previous hip fracture, eating half or less of the food portion offered, and weight monitoring no more than once annually served as covariates, eating snacks predicted the use of vitamin D supplementation in doses of  $\geq 10$  µg (400 IU) (OR 1.65, 95% CI, 1.25-2.17). Weight monitoring no more than once annually (OR 0.47, 95% CI, 0.27-0.81) and malnutrition (MNA score < 17) (OR 0.57, 95% CI, 0.42-0.79) were risk factors for the inadequate use of vitamin D supplements. In this analysis, gender, age, lactose intolerance, poor physical functioning, constipation, and previous hip fracture proved insignificant.



## 5.5 Inappropriate prescribing

### 5.5.1 Polypharmacy

Altogether 40.3 of the nursing home residents consumed  $\geq 9$  drugs daily, a cut-off point for polypharmacy among nursing home residents (Hanlon et al. 2001). No significant difference in exposure to polypharmacy existed between females and males. Residents consuming  $\geq 9$  drugs daily more often had previous stroke ( $p < 0.001$ , 95% CI, -0.125 to -0.04), current depression ( $p = 0.001$ , 95% CI, -0.138 to -0.035) or received psychotropic medication ( $p < 0.001$ , 95% CI, -0.233 to -0.168) than did those consuming  $< 9$  drugs daily. Residents consuming  $\geq 9$  drugs daily were diagnosed with dementia ( $p < 0.001$ , 95% CI, 0.111-0.193) or poor nutritional status (MNA score  $< 17$ ) ( $p < 0.01$ , 95% CI, 0.013-0.093) less often than residents who received  $< 9$  drugs daily.

### 5.5.2 Potentially inappropriate drugs

Of all nursing home residents, 34.4% used PIDs according to the Beers 2003 criteria of potentially inappropriate medication use among older adults independent of diagnoses or conditions (Fick et al. 2003). Of all residents, 5.3% ( $n=105$ ) used two PIDs, 0.7% ( $n=14$ ) used three PIDs, two residents used four PIDs, and one resident used five PIDs simultaneously. Factors associated with PIDs were polypharmacy ( $\geq 9$  drugs daily), psychotropic drug use, and no diagnosis of dementia. Users and non-users of PIDs showed no difference in age, gender, level of education, widowhood, previous stroke, depression, ability to move independently, or malnutrition (see Paper IV: Results).

The most prevalent PIDs in our study population were short-acting benzodiazepines in greater-than-recommended doses (13.9% of all residents), hydroxyzine (7.1%), nitrofurantoin (6.3%), long-acting benzodiazepines (2.4%), and amitriptyline and its combinations (2.2%). Temazepam  $> 15$ mg, used by 13.5% of all residents, accounted for most of the short-acting benzodiazepine use in greater-than-recommended doses. The mean dose of temazepam was 19.1 mg, and the median dose was 20 mg (range 10-40 mg). The three most frequently used PIDs – temazepam ( $> 15$  mg), hydroxyzine, and nitrofurantoin – accounted for 76.9% of all PIDs (Table 9).

**Table 9.** PIDs in nursing homes in Helsinki

Potentially inappropriate drug	Residents using the drug, % (n)
Gastrointestinal antispasmodic drugs:	0.2 (4)
A03BA03 hyoscyamine	
A03CA02 clidinium-chlordiazepoxide	
A06AB02 bisacodyl (without opiate)	0.8 (16)
B01AC07 short-acting dipyridamole	0.75 (15)
B03AA07 ferrous sulphate > 325 mg/day	0.45 (9)
C01AA05 digoxin > 0.125 mg/day (except when treating atrial arrhythmias)	0.7 (14)
C01BA03 disopyramide	0.05 (1)
C01BD01 amiodarone	0.15 (3)
C04AE01 ergot mesyloids	0.5 (10)
G03C estrogens only (oral)	1.15 (23)
J01XE01 nitrofurantoin	6.3 (125)
Non-selective longer half-life NSAIDs in long-term, full-dosage use:	0.45 (9)
M01AE02 naproxen	
M01AC01 piroxicam	
G04BD04 short-acting oxybutynin	1.1 (22)
N02AC04 propoxyphene and comb.	0.3 (6)
N04AB02 orphenadrine	0.35 (7)
N05AC02 thioridazine	0.6 (12)
N05BC01 meprobamate	0.4 (8)
Long-acting benzodiazepines:	2.4 (48)
N05BA02 chlordiazepoxide	
N05BA01 diazepam	
Short-acting benzodiazepines in high doses:	13.9 (276)
N05BA06 lorazepam > 3 mg,	
N05BA04 oxazepam > 60 mg,	
N05BA12 alprazolam > 2 mg,	
N05CD07 temazepam > 15 mg,	
N05CD05 triazolam > 0.25 mg	
N06AA09 amitriptyline and comb.	2.2 (48)
N06AA12 doxepin	0.7 (14)
N06AB03 fluoxetine daily	1.3 (26)
N05BB01 hydroxyzine	7.1 (141)

The table excludes PIDs available in Finland in 2003 but not used among our study population: barbiturates, belladonna alkaloids, clonidine, cyclandelate diphenhydramine, indomethacin, ketorolac, pethidine, methyltestosterone, short-acting nifedipine, and tripeleminamine.

The codes preceding the drug names refer to the ATC code.

## 5.6 Drug-drug interactions

Altogether 4.8% of all residents were susceptible to a class D drug-drug interaction according to SFINX; two residents were susceptible to two class D interactions. Residents exposed to potential DDIs were more likely than others to be younger (mean age 81.8 years vs. 83.8 years,  $p=0.01$ ), to have had a previous stroke (45.6% vs. 29.0%,  $p=0.002$ ), to use psychotropics (89.6% vs. 79.2%,  $p=0.01$ ), to be unable to move independently (40.6% vs. 29.8%,  $p=0.03$ ), to consume a higher number of drugs (9.8 vs. 7.8,  $p < 0.001$ ), and to be exposed to polypharmacy (58.3% vs. 42.0%,  $p=0.002$ ). Of PID users and non-users, 6.6% and 3.9%, respectively, were susceptible to class D interactions ( $p=0.006$ ). Residents exposed to DDIs showed no significant differences in gender, level of education, widowhood, depression, diagnosis of dementia, or malnutrition from residents unexposed to DDIs (see Paper IV: Results).

Of all carbamazepine users ( $n=67$ ), 24% ( $n=16$ ) were exposed to a potential class D DDI. Of codeine users ( $n=63$ ), 21% ( $n=13$ ) used a drug inhibiting the formation of morphine from prodrug codeine. Of potassium users ( $n=314$ ), 11% ( $n=36$ ) used a potassium-sparing diuretic, and were therefore at risk for hyperkalemia. Of warfarin users ( $n=157$ ), 3% ( $n=5$ ) used NSAID simultaneously, thereby increasing their risk for bleeding (see Paper IV: Results).

## 5.7 Prescribing in public and private nursing homes

Residents in private nursing homes were older, more often female, better nourished, and had a higher Charlson comorbidity index than did those residing in public nursing homes (Table 8). Despite these factors, residents in private nursing homes had a lower number of daily drugs than did residents in public nursing homes [7.58 (SD 3.4) vs. 8.28 (SD 3.7)  $p < 0.001$ ] and were less often exposed to polypharmacy (36.6 vs. 44.6,  $p < 0.001$ ). The prevalence of laxatives among residents in private nursing homes was lower than among those in public ones: 52.7% vs. 58.3%,  $p=0.013$ , respectively. No differences existed in the use of psychotropic drugs ( $p=0.87$ ) or potentially inappropriate drugs ( $p=0.91$ ) or exposure to drug-drug interactions ( $p=0.28$ ).

In multivariate logistic regression analysis, in which those factors statistically significant in the univariate analysis served as covariates, residents in private nursing homes were less often exposed to polypharmacy ( $\geq 9$  drugs daily) (OR 0.65, 95% CI, 0.53-0.78).

## 6 Discussion

### 6.1 Study population and methods

The study population for Studies I, II, and IV comprised 1987 aged long-term residents of nursing homes, or 82% of all nursing home residents in Helsinki in 2003; Study III (n=2114) included 87% of all residents. The exclusion criteria were short-term residency, refusal to participate, and insufficient information on drug use. For Studies I, II, and IV, we excluded residents younger than 65 years.

The mean age in Studies I, II, and IV was 84 years, and 83 years in Study III. Of all residents, 28% were malnourished and 60% were at risk for malnutrition. The mean Charlson comorbidity index was 2.12, and the mean number of drugs consumed daily was 7.9. Of all residents, 40% consumed more than nine drugs daily and were exposed to polypharmacy.

The inclusion of all nursing homes in Helsinki and the high response rate provided a reliable picture of prescribing among nursing home residents. Collecting medical data directly from residents' medical records rather than using computerized data records increased the accuracy and reliability of the results. However, errors can occur when completing the questionnaires and entering the data into electronic form. To minimize the coding of errors, a researcher afterwards compared each resident's medication list in the questionnaire to the electronic version of the list. The data were collected without personal identification information and remained anonymous. Identifying residents in order to complete missing information or for future analyses was impossible. Consequently, the cross-sectional study design permits the analysis of associations, not of causalities or trends.

Those residents whose medication records indicated a regular drug administration were classified as drug users. Others, including those residents using a drug on an as-needed basis, were classified as non-users. This may have influenced our results; consequently, drug prevalence may actually be higher. This especially concerns drugs often used on an as-needed basis, such as laxatives, analgesics, or hypnotics. As a result, the association between laxative use and investigated factors may be stronger than reported here. However, the information on as-needed drugs is less reliable than on drugs administered regularly, so as-needed drugs were excluded from the analyses.

Residents with dementia were identified by the diagnoses in their medical records and by the medications they were receiving. Although a large percentage (69.5%) of

residents had received an active diagnosis of dementia, some cases of dementia or other diseases may have gone undetected.

## 6.2 Psychotropic medications

In our study, four in five nursing home residents received psychotropic drugs. The prevalence was high compared to that of international studies, and is probably due to the frequent use of antipsychotics and antidepressants. The use of anxiolytics and hypnotics in our population, however, was moderate compared to that of other studies.

Hypnotics and anxiolytics cause falls and fractures in the elderly (Leipzig et al. 1999, Cumming 1998), and evidence of their impact on behavioral and psychotic symptoms of dementia are lacking (Sink et al. 2005). Consequently, less frequent use of these drugs seems appropriate. The doses of antipsychotics and anxiolytics in our population were considerably lower than those in the Defined Daily Doses (ATC DDD 2009), which is appropriate since DDDs are determined for younger adults and, sometimes, for different indications.

Male residents used conventional antipsychotics and anxiolytics other than benzodiazepines significantly more often than did female residents. The prevalence of SSRIs was higher among female residents. Previous nursing home studies have reported similar findings in the use of antipsychotics and antidepressants (van Dijk et al. 2000, Ruths et al. 2001, Sorensen et al. 2001). Perhaps the more frequent use of antipsychotics in males is due to aggressive symptoms, and perhaps depression among female residents is better recognized in institutional settings. The mean age of male residents was lower in our study, and some researchers have suggested that the lower age of male residents explains the higher prevalence of antipsychotics (Ruths et al. 2001).

The high use of psychotropics in our nursing homes may reflect the overall prescribing culture of psychotropic drugs in Finland. Previous studies have noted the association of facility characteristics with the use of antipsychotics (Hughes et al. 2000), suggesting that the high prevalence of antipsychotics may be related to the low staffing rate in Finnish nursing homes. The mean actual staffing level in nursing homes in Finland has been 0.43 nurses per client on weekdays and 0.35 on weekends (Noro et al. 2005). The National Framework for High-Quality Care and Services for older people suggests a minimum staffing level of 0.5 to 0.6 nurses per client, and a good staffing level is 0.8 nurses per client (Ministry of Social Affairs and Health 2008).

The use of psychotropic drugs also depends on resident characteristics such as dementia, psychiatric diagnoses, and behavioral symptoms. The prevalence of dementia in our nursing homes (70%) is notably higher than that reported in Denmark (Sorensen et al. 2001) and the US (50%) (Pedone et al. 2004). The frequent use of psychotropics among patients with dementia is partly due to the need to control behavioral and psychotic symptoms of dementia, which present the highest risk for institutionalization (Phillips & Diwan 2003). The characteristics, diagnoses, and symptoms of nursing home residents vary widely between countries and complicate international comparisons.

A previous Helsinki study on psychotropic drugs among nursing home residents with dementia (Pitkala et al. 2004) allows for some conservative comparisons, however. In 1999-2000, the prevalence of psychotropic medication among residents with dementia was 87% compared to 80% in 2003. The prevalence of conventional antipsychotics was more than twice as high in 1999-2000 as in 2003 (41% vs. 18%), whereas atypical antipsychotics were used by 13% of residents with dementia diagnosis in 1999-2000 and by 28% in 2003. The prevalences of antidepressants, anxiolytics, and hypnotics among residents with a diagnosis of dementia were 47%, 38%, and 49% in 1999-2000, and 41%, 25%, and 23% in 2003. The Minimum Data Set of Finnish nursing homes suggests that the use of antipsychotics, anxiolytics, and hypnotics is indeed decreasing (Noro et al. 2005).

The diminishing use of psychotropic drugs and the transition from conventional antipsychotics to atypical antipsychotics represent favorable developments. A growing body of evidence suggests that some non-pharmacological therapies may positively affect the treatment of behavioral and psychotic symptoms of dementia and may occasionally serve as an alternative to pharmacological therapy (Thorgrimsen et al. 2003, Burns et al. 2002, Spector et al. 2000). However, many institutionalized patients require pharmacological symptom control (Forbes 1998).

Of those residents with a diagnosis of dementia, 3% received AChE in 1999-2000 (Pitkala et al. 2004), and 10% in 2003. The use of AChE still seems to be less frequent than in US nursing homes, however. In a study taking advantage of the Minimum Data Set (N=174 659), 30% of newly admitted residents with mild to moderate dementia received donepezil (Pedone et al. 2004). AChEs favorably affect behavioral and psychotic symptoms of dementia (Rosler 2002, McKeith et al. 2000, Tariot et al. 2000), and have been recommended as the primary medication for this indication (Sink et al. 2005). The main indication of AChEs in Finland has previously been related to the care of patients with dementia in order to postpone their institutionalization. This indication, and its high cost, has discouraged the use of

AChEs in nursing homes. Accumulating evidence indicates that AChEs benefit patients with dementia, even at severe stages of the disease, as well as those already institutionalized (Tariot 2003).

Those residents with no diagnosis of dementia received even more psychotropic drugs than did those with a diagnosis of dementia (85% vs. 78%); such residents received antidepressants, long-acting benzodiazepines, and hypnotics significantly more often. Some studies have suggested that depression in residents with a diagnosis of dementia is poorly recognized and undertreated (Elmstahl et al. 1998). Those residents with no diagnosis of dementia include psychiatric patients and, probably, undiagnosed dementia patients. However, the overall high use of psychotropics suggests a need to review the indications themselves.

### 6.3 Laxatives

More than half of nursing home residents used at least one laxative regularly. Osmotic laxatives were the most common. Stimulant laxatives were prescribed for 14% of residents, and more than one in ten residents used at least two regularly administered laxatives simultaneously.

In multivariate logistic regression analysis, advanced age, inability to move independently, a high number of drugs, malnutrition, chewing problems, and Parkinson's disease were associated with laxative use. Eating snacks between meals was associated with lower risk for laxative use. Of the potentially constipation-inducing drugs, several medications were significantly associated with regular laxative use.

The prevalence of laxative use in nursing homes in Helsinki is very similar to that of previous international studies (van Dijk et al. 1998, Harari et al. 1995, Monane et al. 1993, Brocklehurst et al. 1999). In the US, 54% of nursing home residents used laxatives, and 26% of all residents received bulk laxatives, 18% osmotic laxatives, and 16% stimulant laxatives (Phillips et al. 2001). In Britain, 60% of residents received laxatives more than once weekly. Of all residents, 34% used lactulose, and 22% senna (Brocklehurst et al. 1999).

As in some previous studies (van Dijk et al. 1998, Harari et al. 1995, Monane et al. 1993), laxatives served as a proxy drug for constipation, even though the MNA questionnaire included a question inquiring whether the resident experiences constipation. In a population with a high prevalence of laxatives, studying constipation is challenging; as a result, we focused on its consequence: the use of laxatives. Laxatives are seldom used for any other indication than constipation.

However, we do not know whether all laxative users in our study population meet the diagnostic criteria for constipation, and if all residents with constipation receive laxatives.

Eating snacks between meals was associated with lower risk for chronic laxative use in multivariate logistic regression analysis. In Finland, a typical snack includes rye bread with a topping, or a dairy product such as yoghurt. Dark rye bread is rich in fiber, and dairy products contain lactose, which acts as an osmotic laxative. Snacks can also influence laxative use by increasing bulk in the gastrointestinal tract.

In a Norwegian nursing home study, the use of laxatives was associated with the concurrent use of opioids, anti-parkinsonian drugs, and the total number of drugs used, but not with the use of drugs with anticholinergic properties (Nygaard et al. 2003). The constipation-inducing characteristics of opioids, antacids, diuretics, tricyclic antidepressants, histamine-2 blockers, and anticholinergic drugs used for urine incontinence are well known. However, the association between laxative use and non-selective NSAIDs and calcium channel blockers other than verapamil and nifedipine proved interesting. Yet, the constipation-inducing characteristics of NSAIDs, which inhibit the normal production of prostaglandins, appear in the literature (Romero et al. 1996).

The high prevalence of constipation in nursing home residents is, of course, only partly due to ADRs. In a Dutch nursing home study in which laxative use served as a proxy for constipation and each resident underwent a prescription sequence analysis, only those drugs that, according to their product summaries and the literature, exhibit a moderate to strong constipating effect correlated with laxative use (van Dijk et al. 1998). Residents with depression, diabetes mellitus, or relatively good mobility showed a higher risk for drug-induced constipation. Calcium and ferrous salts, and verapamil correlated with constipation (van Dijk et al. 1998). The association between a certain drug and a laxative may stem from the disease for which the drug is prescribed, a symptom of this disease (e.g. immobility), or the constipation-inducing characteristic of the drug.

Essential keystones in treating constipation are a sufficient supply of fluids and fiber, exercise, or physical activity, fiber-containing snacks, and, if needed, laxatives. Using one drug to treat the adverse drug reaction of another is undesirable (Harari et al. 1995). Nursing home residents use many drugs and therefore require frequent evaluation of their mediations.



## 6.4 Vitamin D and calcium supplements

Regardless of the recommendation of vitamin D supplementation to all institutionalized older people, less than one third of nursing home residents received vitamin D, and even fewer received calcium. Only one in five residents received both vitamin D and calcium. Eating snacks between meals, being well nourished, and regular weight monitoring were associated with the use of vitamin D supplements.

Because Finland is located at high northern latitudes, the population's exposure to sunshine is limited during most of the year. In addition, older people residing in institutions spend most of their time indoors regardless of the season. In addition, the cutaneous intake of cholecalciferol decreases with age (Heaney 2004).

Our study indicates that recommendations for vitamin D supplementation are poorly implemented in practice. Reasons for not complying with recommendations may be numerous. Nursing homes may be attempting to avoid polypharmacy or to reduce medication costs, residents may be experiencing difficulties taking the supplements, or the recommendations are simply being ignored.

An increasing body of evidence shows that vitamin D supplementation plays a role in preventing falls and fractures, and the supplementation dose should be at least 800 IU (20µg) daily (Bischoff-Ferrari et al. 2005, Bischoff-Ferrari et al. 2004a, Bischoff-Ferrari & Dawson-Hughes 2007, Venning 2005, Broe et al. 2007). The recommendation of vitamin D supplementation for institutionalized elderly has recently been updated to 800 IU (20µg) (Suominen et al. 2010). Whether the new recommendation will raise the prevalence of vitamin D supplementation among nursing home residents remains to be seen. At present, vitamin D supplements are over-the-counter drugs. The availability of a prescription preparation of vitamin D could affect prescribing patterns.

## 6.5 Potentially inappropriate drugs

One third of nursing home residents in Helsinki received PIDs according to the Beers 2003 criteria. Of particular concern was the proportion of residents receiving more than one PID simultaneously (6%). PID users were more likely to have polypharmacy, psychotropic drugs, and no diagnosis of dementia than were those not receiving PIDs.

The most prevalent PID was temazepam in greater doses than recommended. Temazepam is a benzodiazepine with a half-life of 5 h to 20 h (Pharmaca Fennica 2010). In Finland, temazepam generally serves as a hypnotic administered in the

evening. Nitrofurantoin, which in Finland is used for the short-term treatment of acute urinary tract infections, is considered inappropriate for older adults because of its potential for renal impairment (Fick et al. 2003), nitrofurantoin-induced pulmonary toxicity (Witten 1989), or ineffectiveness in renal impairment (Kunin 2004). The frequent use of hydroxyzine, an antihistamine with strong anti-cholinergic properties, is inappropriate indeed.

The Beers criteria classify bisacodyl, cascara sacra, and castor oil as stimulant laxatives inappropriate for use in older adults, except when co-administered with opiates. Of these, only bisacodyl was used in Finland in 2003, and less than one percent of residents was exposed to stimulant laxatives without receiving opiates simultaneously. If, however, we include in the analysis other stimulant laxatives available in Finland in 2003, then 12% of residents were receiving stimulant laxatives. This demonstrates a focal problem in compiling explicit criteria: applying the criteria in another country may be difficult.

Several previous studies have reported PID use according to the Beers criteria among nursing home residents. Although these studies show a wide range of prevalence in PID use, direct comparison is difficult because the criteria are often modified for local conditions.

In an earlier Finnish study, the prevalence of PIDs among institutionalized older people in 1999-2000 was strikingly similar to that in the present study (36.2% vs. 34.4%) (Raivio et al. 2006). Interestingly, after a two-year follow-up, the study group found no difference in the number of acute hospital days, hospital admissions, or mortality curves between PID users and non-users. The results concerning the adverse drug events of PIDs, according to the Beers criteria, have indeed been contradictory (Spinewine et al. 2007, Wagner et al. 2007, Lau et al. 2005).

Our study used explicit criteria to assess PID prescribing, and the study design allows no use of clinical judgement to evaluate the appropriateness of prescribing for an individual patient. In addition, using explicit criteria in a cross-sectional study enabled us to determine the prevalence of potentially inappropriate drugs, but not the actual outcome of potentially inappropriate prescribing. Sometimes, prescribing a potentially inappropriate drug is actually appropriate. Best current practice for prescribing for geriatric patients relies on the regular evaluation of the safety and efficacy of each medication and medication combination (Hilmer et al. 2007b). Even though polypharmacy carries several disadvantages, reducing the number of drugs is difficult (Pitkala et al. 2001).

## 6.6 Drug-drug interactions

Less than 5% of the nursing home residents in Helsinki were susceptible to potential clinically significant drug-drug interactions. Residents exposed to DDIs were more likely to use PIDs and to be exposed to polypharmacy.

More than half of the DDIs in our study population presented a risk for losing the treatment effect. However, some of the DDIs may lead to a dramatically adverse outcome. The simultaneous use of warfarin and NSAIDs (five residents) is of particular concern indeed. Seven residents were exposed to a DDI that could potentially cause a cardio-depressive effect, and 36 residents were exposed to a DDI that could lead to hyperkalemia. The latter is perhaps not so problematic in a nursing home setting, since the residents can be followed up for their pulse, electrocardiograms, and serum potassium. However, the majority of the remaining DDIs in our population could lead to a loss of treatment effect, which may lower the resident's quality of life.

A large Swedish study investigating potential DDIs from the prescriptions of over 8000 home-dwelling individuals, found that age and polypharmacy correlated positively with DDIs (Astrand et al. 2006). Of all the potential DDIs detected, clinically significant class D interactions constituted 8%. The study utilized the Swedish classification system of DDIs ([www.fass.se](http://www.fass.se)), which preceded the SFINX database and is embedded in it.

A study performed in six European countries and using the same Swedish classification system reported a prevalence of class D DDIs among elderly outpatients ranging from 4% to 12%. The most common DDIs in this study were ipratropium bromide and  $\beta$ 2-agonists, potassium and potassium-sparing agents, and antithrombotic agents combined with NSAIDs or acetylsalicylic acid (Bjorkman et al. 2002).

Some authors have suggested that to avoid drug interactions and compliance problems, drug regimes for older people should remain as simple as possible and the goal should be one or two treatments daily (Turnheim 2004). The primary question in prescribing for the elderly should not be which drug to choose or how to administer it, but whether the drug is actually necessary (Turnheim 2004). Simpler drug regimens may be achieved by prescribing drugs that can be taken once daily and or by choosing a combination pill when adding a second drug (Lee 1998).

Fortunately, a potential interaction does not necessarily lead to an actual adverse outcome. Assessment of actual interactions is based on clinical judgement (Mallet et al. 2007) or, in some cases, laboratory tests. Tools for screening potential interactions

are important for the prevention of actual ones. Computerized interaction programs such as SFINX may help the professional to identify patients susceptible to interactions, but do not substitute for clinical knowledge (Saarelma et al. 2006). SFINX points out the pharmacokinetic interaction of two drugs, but does not warn of parallel or contrary drug effects (Saarelma et al. 2006).

## 6.7 Public and private nursing homes

Of all residents, 46% were residing in public, and 54% in private nursing homes. Residents in private nursing homes were older, more often female, and had higher MNA scores and Charlson comorbidity indices than did residents in public nursing homes. Several morbidities predispose people to polypharmacy, yet residents in private nursing homes were less often exposed to polypharmacy than were residents in public nursing homes. Avoiding polypharmacy is indeed appropriate. However, these data do not enable one to evaluate the appropriateness of prescribing on the level of the individual resident, so potential underuse or overuse often remains undetected. In addition, we do not know whether these institutions follow identical practices in maintaining their medication records.

The new Act on Public Procurement took effect in 2007 ([www.finlex.fi](http://www.finlex.fi)). This act defines the standards for the procurement of goods and services in public administration, including nursing home services publicly funded as a part of the Finnish social security and health care system. The data for this study were collected in 2003, and the new act may have affected the quality of services purchased from the private sector since the data collection.

## 6.8 Perspectives on prescribing in nursing homes

This cross-sectional study describes the use of psychotropic drugs, laxatives, vitamin D and calcium supplements, and potentially inappropriate drugs as well as exposure to clinically significant drug-drug interactions in nursing homes. Although the study design does not allow for assessment of the appropriateness of prescribing at the level of the individual resident, using explicit criteria and assessing drug prevalence, along with factors associated with drug use, nevertheless provide us with a comprehensive picture of drug therapy among nursing home residents.

A more detailed picture of prescribing, including overprescribing and underprescribing at the level of the individual resident level, could be achieved with implicit criteria and the geriatric assessment of residents' diagnoses and prescriptions.

However, such a methodology is time-consuming and laborious, and would thus be feasible only for a smaller sample representative of all nursing home residents.

In Helsinki, the use of psychotropic drugs is much more common than figures for international nursing indicate. This disparity is partly due to patient characteristics, but nevertheless raises concerns over the appropriateness of indications for psychotropic drug use. In many cases, psychotropic drugs are necessary and form an integral part of appropriate treatment. However, we should pay close attention to the indications for psychotropic drug use every time they are prescribed or when assessing a resident's existing medication record.

Residents eating snacks between meals used laxatives less often than did residents who ate no such snacks. Good nutritional care can indeed impact one's need for drugs. Vitamin D and calcium supplementation are easy and simple means to ensure an adequate supply of necessary micronutrients. Adhering to the national guidelines of vitamin D supplementation for institutionalized older people should be self-evident.

Due to the anonymous data of nursing home residents in the present study, a real follow-up study would be inappropriate. Changes in prescribing practices could be investigated, however, even though the medication records of individual residents cannot be linked. For example, changes in the prevalence of AChEs and other psychotropics among residents with a diagnosis of dementia would be an especially interesting topic for future study.

Criteria for appropriate or good-quality drug use are useful aids for clinical decision-making. They should, however, be considered suggestions, not rules, for proper prescribing. Rather than focusing on diseases or blindly following guidelines, the prescriber should concentrate on the unique medication needs of each individual patient and aim for optimal drug therapy which meets the individual patient's needs. Especially when treating older patients, the indication, choice, dosage and duration of each medication and medication combination must be carefully thought through.

## 7 Conclusions

The prevalence of psychotropic drugs among nursing home residents is very high. In addition, many nursing home residents are exposed to polypharmacy. Regardless of the national recommendations for vitamin D supplementation, the prevalence of vitamin D and calcium supplementation is alarmingly low. Three of the most frequently prescribed potentially inappropriate drugs for older adults, according to the Beers criteria, comprise more than three quarters of all potentially inappropriate drugs. Potentially clinically significant drug-drug interactions seem not to be a focal problem in nursing homes, and the prevalence of laxatives seems to be in line with that in international studies. The quality of drug therapy may be higher in private nursing homes than in public nursing homes.

Paying close attention to proper indications of psychotropic drugs would likely improve the quality of psychotropic prescribing in nursing homes. So would replacing potentially inappropriate drugs with more appropriate ones. Moreover, adhering to the guidelines of vitamin D supplementation for elderly institutionalized people in all nursing homes should be self-evident.

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## Appendix 1



## ASUKKAAN RAVITSEMUSTILAN ARVIOINTI (MNA) 20.1.2003

Anna tutkimallesi asukkaalle **numero**, \_\_\_\_\_, laita annetulle listalle muistiin asukkaan numero,

nimi ja sotu. Säilytä lista osastolla.

Vanhainkoti: \_\_\_\_\_, no: \_\_\_\_\_

Osasto: \_\_\_\_\_, **no**: \_\_\_\_\_

Vanhainkoti on: kaupungin oma \_\_\_\_\_, ostopalvelu \_\_\_\_\_

Päivämäärä: \_\_\_\_\_

Pituus \_\_\_\_\_ cm

Paino nyt \_\_\_\_\_ kg, paino syksyllä 2002 \_\_\_\_\_ kg

Kantapää-polvi \_\_\_\_\_ cm

Kuinka kauan asukas on ollut kyscissessä vanhainkodissa? \_\_\_\_ vuotta \_\_\_\_ kuukautta

Seuraavissa kysymyksissä ympyröi yksi vastausvaihtoehtoista ja kirjaa ympyröimäsi numero kysymyksen oikealla puolella olevaan ruutuun.

### SEULONTA

1. Onko ravinnonsaanti vähentynyt viimeisen kolmen kuukauden aikana ruokahaluttomuuden, ruoansulatusongelmien, puremis- tai nielemisvaikeuksien takia?

0 = Kyllä, ravinnonsaanti on vähentynyt huomattavasti

1 = Kyllä, ravinnonsaanti on vähentynyt hieman

2 = Ei muutoksia

2. Painonpudotus kolmen viime kuukauden aikana?

0 = Painonpudotus yli 3 kg

1 = Ei tiedä

2 = Painonpudotus 1-3 kg

3 = Ei painonpudotusta

3. Liikkuminen?

0 = Vuode- tai pyörätuolipotilas

1 = Pääsee ylös sängystä, mutta ei käy ulkona

2 = Liikkuu ulkona

4. Onko viimeisen kolmen kuukauden aikana ollut psyykkistä stressiä tai akuutti sairaus?

0 = Kyllä

2 = Ei

5. Neuropsykologiset ongelmat?

0 = Dementia, depressio tai neuropsykologinen ongelma

1 = Lievä dementia, depressio tai neuropsykologinen ongelma

2 = Ei ongelmia

6. Painoindeksi eli BMI (=paino / (pituus)<sup>2</sup> kg/m<sup>2</sup>)

0 = BMI on alle 19

1 = BMI on 19 tai yli, mutta alle 21

2 = BMI on 21 tai yli, mutta alle 23

3 = BMI on 23 tai enemmän

**Pisteet yhteensä (1. sivu)**

## ARVIOINTI

7. Asuuko haastateltava kotona?

0 = Ei

1 = Kyllä

8. Onko päivittäisessä käytössä enemmän kuin 3 reseptilääkettä?

0 = Kyllä

1 = Ei

9. Painehaavaumia tai muita haavoja iholla?

0 = Kyllä

1 = Ei

10. Päivittäiset lämpimät ateriat (sisältää puurot ja vellit)?

0 = 1 ateria

1 = 2 aterialla

2 = 3 aterialla

11. Sisältääkö ruokavalio vähintään

Ei    Kyllä

- Yhden annoksen maitovalmisteita

(maito, juusto, piimä, viili) \_\_\_\_

- Kaksi annosta tai enemmän kananmunia

viikossa (myös ruuissa, esim. laatikot) \_\_\_\_

- Lihaa, kalaa tai linnun lihaa joka päivä \_\_\_\_

0 = Jos 0 tai 1 kyllä -vastausta

0.5 = Jos 2 kyllä -vastausta

1 = Jos 3 kyllä -vastausta

12. Kuuluuko päivittäiseen ruokavalioon kaksi tai useampia annoksia hedelmiä tai kasviksia?

0 = Ei

1 = Kyllä

13. Päivittäinen nesteen juonti?

0 = Alle 3 lasillista

0.5 = 3-5 lasillista

1 = Enemmän kuin 5 lasillista

14. Ruokailu

0 = Tarvitsee paljon apua tai on syötettävä

1 = Syö itse, mutta tarvitsee hieman apua

2 = Syö itse ongelmitta

15. Oma näkemys ravitsemustilasta

0 = Vaikea virhe- tai aliravitseminen

1 = Ei tiedä tai lievä virhe- tai aliravitseminen

2 = Ei ravitsemuksellisia ongelmia



16. Oma näkemys terveydentilasta verrattuna muihin samanikäisiin

0 = Ei yhtä hyvä

0.5 = Ei tiedä

1 = Yhtä hyvä

2 = Parempi

17. Olkavarren keskikohdan ympärysmitta (OVY cm)

0 = OVY on alle 21 cm

0.5 = OVY on 21-22 cm

1.0 = OVY on yli 22 cm

18. Pohkeen ympärysmitta (PYM cm)

0 = PYM on alle 31 cm

1 = PYM on 31 cm tai enemmän

**Pisteet yhteensä (2+3. sivu)**

Pisteet yhteensä 1. sivulla

**Kokonaispistemäärä**

## ASUKKAAN TAUSTATIEDOT

Kysymyksien vastausvaihtoehdoista ympyröidään sopivin numero (vain yksi).

19. Ikä: \_\_\_\_\_ vuotta

20. Sukupuoli?

1 = Nainen

2 = Mies

21. Siviilisääty?

1 = Naimaton

2 = Leski

3 = Eronnut

4 = Avio- tai avoliitossa

22. Koulutus?

1 = Kansakoulu tai vähemmän

2 = Ammattikoulu

3 = Keskikoulu

4 = Lukio

5 = Opistoasteen ammattikoulutus

6 = Korkeakoulu

23. Minkälaisessa työssä asukas on toiminut pääsääntöisesti elämänsä aikana?

1 = Maanviljelys, karjanhoito, metsätyö, emännän työt

2 = Tehdas-, kaivos-, rakennus-, tai muu vastaava työ

3 = Toimistotyö, henkinen työ, palvelutyö

4 = Muu, mikä? \_\_\_\_\_

24. Mikäli yksikössä on käytössä RAI, mitkä ovat asukkaan viimeisimmän RAI – mittauksen tulokset?

1 = CPS \_\_\_\_\_

2 = BMI \_\_\_\_\_

3 = ADL \_\_\_\_\_

4 = Kipuskaala \_\_\_\_\_

5 = Masennuskaala \_\_\_\_\_

25. Onko asukkaalla joku erityisruokavalio?

Ei

Kyllä

1 = Laktoositon 1 2

2 = Keliakia 1 2

3 = Diabetes (insuliini) 1 2

4 = Diabetes (ei insuliini) 1 2

5 = Sappi 1 2

6 = Kihti 1 2

7 = Kasvis 1 2

8 = Muu, mikä \_\_\_\_\_ 1 2

26. Minkä verran asukas syö pääaterioiden suositellusta annoskoosta keskimäärin?

1 = Vähemmän kuin puolet

2 = Puolet

3 = Lähes kaiken

4 = Kaiken

27. Millainen on asukkaan ruoan rakenne?

1 = Nestemäinen

2 = Sosemainen

3 = Pehmeä

4 = Kiinteä

28. Syökö asukas välipaloja?

1 = Ei

2 = Kyllä

29. Käytetäänkö asukkaalla täydennysravintovalmisteita (esim. Nutrison, Semper, Fortimel, Ensini, Additene jne.)?

1 = Ei

2 = Kyllä

30. Saako asukas kalkkivalmistetta

1 = Ei

2 = Kyllä

31. Saako asukas D-vitamiinivalmistetta

1 = Ei

2 = Kyllä

32. Kuinka usein asukkaan paino mitataan keskimäärin?

1 = Ei koskaan

2 = Kerran vuodessa tai harvemmin

3 = Kahdesti - kuudesti vuodessa

4 = Yli kuusi kertaa vuodessa

33. Kirjataanko asukkaan vatsantoiminta?

1 = Ei

2 = Kyllä

34. Onko asukkaalla seuraavia ruokailuun ja suuhun sekä ruoansulatuselimistöön liittyviä ongelmia? Ei Kyllä

1 = Puresmisongelmia 1 2

2 = Kuiva suu 1 2

3 = Kipua suussa 1 2

4 = Nielemisongelmia 1 2

5 = Ummetusta 1 2

6 = Ripulia 1 2

7 = Oksentelua 1 2

8 = Ruoalla sotkemista/ruoan pois työntämistä tai 1 2  
sylkemistä/malttamattomuutta syödessä

9= Muita ongelmia, mitä \_\_\_\_\_ 1 2

35. Mikä on asukkaan hampaiston tila syödessä?

1 = Hampaaton, ei proteesia

2 = Kokoproteesi sekä ylä- että alaleuassa

3 = Hampaaton, mutta joko ylä- tai alaleuan kokoproteesi ja/tai muita osaproteeseja

4 = Omia hampaita ja yksi tai useampia proteeseja

5 = Vain omia hampaita

36. Onko asukkaalla seuraavia sairauksia tai onko asukas sairastanut aikaisemmin?

Ei    Kyllä

1 = Sokeritauti 1 2

2 = Sepelvaltimotauti 1 2

3 = Sydänveritulppa eli sydäninfarkti 1 2

4 = Aivohalvaus tai aivoverenkiertohäiriöitä 1 2

5 = Dementia 1 2

6 = Parkinsonin tauti 1 2

7 = Maha- tai pohjukaissuolen haavauma 1 2

8 = Muu krooninen suolistosairaus 1 2

• Jos on, mikä \_\_\_\_\_

9 = Lonkkamurtuma 1 2

10. = Syöpä 1 2

• Jos on, mikä \_\_\_\_\_

• Jos on, milloin todettu \_\_\_\_\_

11. = Jokin muu pitkäaikainen sairaus 1 2

• Jos on, mikä \_\_\_\_\_

37. Aukkkaan säännöllisesti käyttämät, lääkäriin määräämät lääkkeet ja vitamiinit. (Kirjoita alla olevaan tilaan valmisteiden nimet tai kopioi lääkelista ilman asukkaan nimeä ja henkilötunnusta ja näyttää se tämän lomakkeen perään.)

1 = \_\_\_\_\_

2 = \_\_\_\_\_

3 = \_\_\_\_\_

4 = \_\_\_\_\_

5 = \_\_\_\_\_

6 = \_\_\_\_\_

7 = \_\_\_\_\_

8 = \_\_\_\_\_

9 = \_\_\_\_\_

10. = \_\_\_\_\_

11. = \_\_\_\_\_

12. = \_\_\_\_\_

13. = \_\_\_\_\_

14. = \_\_\_\_\_

15. = \_\_\_\_\_

16. = \_\_\_\_\_

17. = \_\_\_\_\_

18. = \_\_\_\_\_

19. = \_\_\_\_\_

20. = Listaa kaikki muut lääkkeet: \_\_\_\_\_

Lomakkeet palautetaan yhdessä osastonhoitajan täyttämän lomakkeen kanssa \_\_\_\_\_  
mennessä Vanhusten laitos- ja asumispalveluihin.

Original publications